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FIG. 1.—Casal's illustration of cutaneous lesions in pellagra.

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ORIGINAL ARTICLES.

PELLAGRA AND SOME OF ITS PROBLEMS.<sup>1</sup>

By JAMES NEVINS HYDE, M.D.,

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EXTENDED research on the part of scientific men, physicians and others, in the several countries of Europe where pellagra has long prevailed, has resulted in the production of a literature that is as vast as it is illuminating. The relatively recent appearance of the disease on this side of the Atlantic has awakened a special interest in the subject, not merely among American observers, but also among authorities, both Italian and English, who have learned with no little surprise of the new chapter to be written in this century on the history of the disorder. In the limits of the present paper only the briefest reference can be made to the labors

<sup>1</sup> The record of neurological symptoms in the patients described in this paper was made by Peter Bassoe, M.D., assistant professor of nervous and mental diseases in the Rush Medical College; and the record of blood-findings, including the bacteriology in nine patients, was made by D. J. Davis, M.D., instructor in pathology and medicine in Rush Medical College. The author is greatly indebted to these gentlemen for these reports, and desires to express his thanks to Dr. J. W. Babcock, physician and superintendent of the State Hospital for the Insane, Columbia, South Carolina, for the privilege of examining pellagra patients, both public and private, during the session of the National Pellagra Conference held in that city on November 3 and 4, 1909; and unites with his collaborators in acknowledging obligations to Dr. George A. Zeller and Dr. George Michell, of the Peoria State Hospital for the Insane, Bartonville, Illinois, for permission to observe and make special study of pellagrous patients in that institution; also to Dr. V. H. Podstata, superintendent and physician of the Hospital for the Insane at Elgin, Illinois; and to Dr. L. J. Pollock, physician of the Cook County, Illinois, Asylum for the Insane, for the opportunity of making examination of other pellagrous patients in these institutions.

of the authors whose names have been identified with the study of the malady. The attempt is here made briefly to sketch, as far as may be, the phenomena of the disease as they have been recognized in this country, and incidentally to formulate some of the problems with which the students of pellagra in the United States apparently are confronted.

Many of the several names which have been given to the disease reflect the opinions once prevalent respecting its nature and cause. It has been termed *Mal de la Rosa*, *Risipola Lombarda*, *Lombardy Erysipelas*, *Lepra Italica*, *Alpine Scurvy*, *Mal Rosso*, *Mal Roxo*, *Maïdica*, *Psychoneurosis Maïdica*, *Maladie de la Teste*, *Malattie della Miseria*, *Mal de Sole*, *Mal de Asturias*, *Raphania Maistica*, *Malattia dell' Insolato di Primavera*; and other titles have been employed in its designation. Though vaguely recognized before his time, the first authentic description of the disease was made by a Spanish physician, Gaspar Casal, under the title *Mal de la Rosa*, the fruit of observation made by him among the peasants of the Asturias in the year 1735. His work was written in the Latin tongue, and published after his death by Joseph Garcia in the year 1762. In this monograph the portrait (Fig. 1) illustrating the localization of the disease correctly represents its cutaneous stigmas as they are betrayed today. His description of the pellagrous skin is noticeably accurate: "*Degenerat tandem in crustam siccissimam, scabrosam, nigricantem, profundis sæpissime interciissam fissuris, etc.*"

Frapolli, of Milan, in 1771, is commonly reported as first to have given the name to the disease by which today it is most generally known, but in fact he merely reproduced a title current among the people of his day: "*Morbus, vulgo, Pellagra.*" In the long list of authors who followed, from Strambio, Marzari, Alibert, Rayer, and Raymond, to Lombroso, Sandwith, Babes and Sion, and Sir Patrick Manson, can be traced the progress of the disease in Europe from Spain to Southern France, northern and central Italy, Corfu, upper Egypt, and other parts of Africa, Austria, Servia, Bulgaria, Roumania, Asia Minor, India, Mexico, Barbadoes, and portions of North and South America.

The prevalence of the disorder in Europe may be estimated to a degree from its ravages in Italy, which has suffered more than any one other country. In Lombardy alone from the year 1770, when attention was first paid to the serious character of the endemic, to the year 1880 the number of pellagrins increased from 20,000 to 104,067. It has been estimated that in a population of 16,689,735, of northern and central Italy, the proportion of those affected with the disease rose from one in sixty to one in nineteen of the inhabitants. At the present time, thanks to the extraordinary efforts of the Government in the matter of improving the hygienic and especially the dietetic habits of the peasantry, a marked decrease

has been accomplished in the number of fresh cases of the disease; and in a few districts where there was a readiness to conform to the regulations provided by the State, it is reported that pellagra has been practically eradicated.

The great multiformity in the symptoms displayed in different cases, and the obvious influence of the rays of solar light in the production of certain of the cutaneous phenomena, have led several authors to an opinion, formulated by Winternitz in 1876, that there is not a nosological entity which corresponds to the term pellagra. Bonnet, four years later, and other writers, descanting upon supposed cases of "pseudopellagra," lean to the same conclusion, a conclusion which seems to have been shared by several modern observers, and which gave weight to the French aphorism that pellagrins are "*des malades sans une maladie*." Reference is made to this opinion chiefly with a view to emphasizing the fact that pellagra, as its phenomena have been unfolded before the clinicians of our day, is a disorder of admitted contradictions, of complexity of morbid symptoms, of strange subversions of any determinate order of evolution. Yet, all said and done, a conscientious study of the disease leads to the conviction that pellagra, in its complexus of symptoms, is a distinct affection, resembling none other, and, despite irregularity in the order of its manifestations impressed with a definite and characteristic physiognomy. Its poison, though as yet unrecognized, is probably one; the effects of that poison, operating upon a wide field of the human economy, wider than in most of the serious endemic maladies of the human family, are many.

Pellagra is neither infectious, contagious, nor inherited. In countries where labor in the fields is accomplished chiefly by men, these suffer more than women. Elsewhere, the subjects of the disease are in larger proportion women. The one chief predisposing factor in its production is, without question, the asthenic condition of a poverty-stricken, poorly nourished, and enfeebled class of subjects. Though not inherited, pellagra may affect children at an early age; the larger number of patients, however, develop its symptoms between the close of the second and of the fifth decade of life. That it is a disorder chiefly developed in warm countries can scarcely be doubted apart from the arguments adduced in favor of its close connection with the crops raised within certain fixed geographical limits. The southern portions of Europe have unmistakably suffered more than those in the extreme north. The probable geographical limits lie between 40° and 50° north latitude.

The effects of pellagrous intoxication of the human body are exerted chiefly in three systems of the economy—the nervous, the cutaneous, and the gastro-intestinal. The order and importance of these is not exactly determined. Examining the three from different points of view, authors have attributed sometimes to one



of these and again to another a chief importance. But the cutaneous symptoms have not only given to pellagra its most commonly employed designation (Ital., *pelle*, skin; *agra*, rough), but, further, have furnished its most constant and determinate features. It is possible that there may be a *pellagra sine pellagra*, but few clinicians would venture to make a diagnosis of this sort in any sporadic case beyond the limits of a pellagrous district.

The classical type of pellagra recognized in Europe may be briefly described as follows (the American variations from the Italian and Egyptian portraits will be noticed in passing):

The question of a distinct prodromal period introduces at once to the confusion which has prevailed respecting many features of the disorder. By some it is believed that year after year, before the first unmistakable symptoms are betrayed, the patient experiences an increasing sensation of languor and of general malaise. It is clear, however, that even in the class of subjects who tolerate minor ailments with relative equanimity, in the early spring season of the year there is experienced an unwonted lassitude, vertigo, epigastric pain, bowel looseness, and inappetence. Often there is coincident involvement of the tongue, which may be coated, or become reddened and studded with prominent papillæ. More rarely there are superficial losses of its enveloping membrane, and in extreme cases, ulceration of the mucosa. Other uncomfortable symptoms experienced at this period are more or less severe headache, accompanied by vomiting. Pellagra has been described as a feverless disease. The temperature throughout may be normal. Again, by one of those odd anomalies which frequently are to be recognized in the course of the disease, all the gastro-intestinal symptoms may be ameliorated at the date of the onset of the cutaneous efflorescence. As the eruptive phenomena are practically alike in patients affected with pellagra on both sides of the Atlantic, the following may be held to be fairly descriptive of the average of cases, wherever observed. For the convenience of classification of symptoms, three stages are described by writers.

The eruption (pellagrous erythema) in the first stage develops, as a rule, suddenly and with practical symmetry, in the days of early spring, and is commonly limited to the uncovered parts of the body exposed to the sun's rays (the face, neck, hands, and, in those not clothing the lower limbs, also the feet). The entire face may be symmetrically involved, producing thus the pellagrous "mask" (Fig. 2). Often, however, portions only of the face are involved; the brow may be spared in men who wear hats; while in insane women, whose faces are less protected, we have seen characteristic "welts" across the upper portion of the forehead. In both sexes it is not rare to see the beardless chin involved; occasionally the cheeks also, to the exclusion of other parts.

The erythematous circlet about the neck (Ger., *Casal'sche*

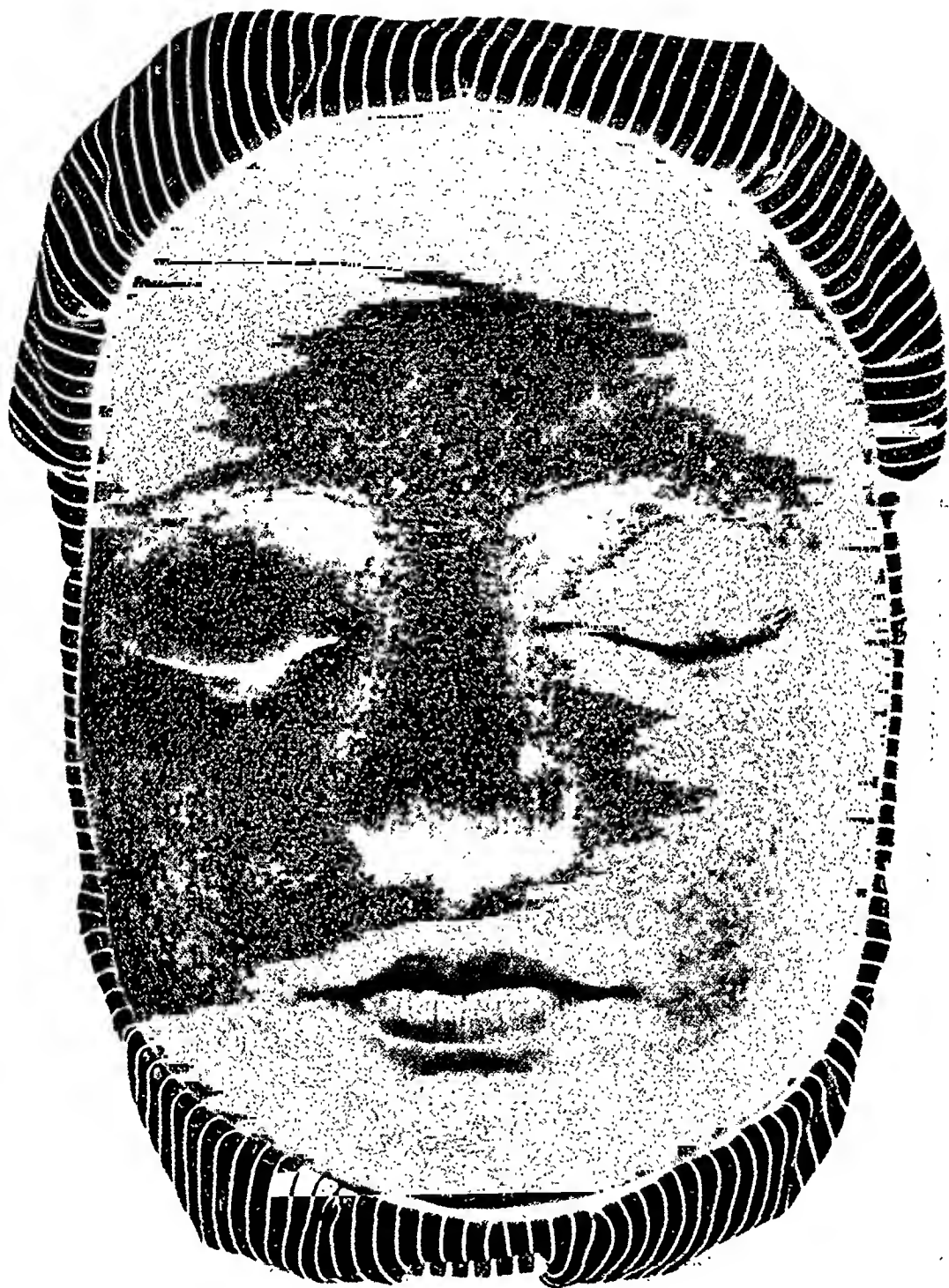


FIG. 2.—Pellagrous “mask” of the face. (Reproduced through the courtesy of Prof. Ludwig Merk, of Innsbruck.)



*Halsband*; Ital., *Il collare pellagroso*), first depicted by Casal, is one of the characteristic stigmas of the disease. In front, distinct lines of demarcation can usually be recognized at the lower border of the "collar," representing the line of contact of the shirt or other garment protecting the inferior part of the neck. The upper border of the "collar" in front is often as distinctly outlined by reason of the protection from sunlight furnished by the chin. Behind, the "collar" stretches from the clothing below to the line of the hairs of the occiput. The ears may be simultaneously affected.

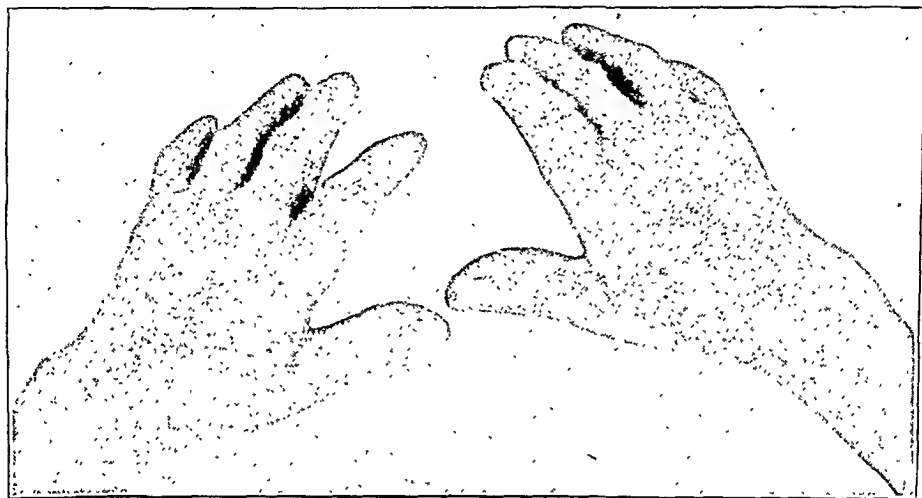


FIG. 3.—Pellagrous erythema of the hands. Patient not insane. (Courtesy of Dr. Michell.)

The dorsa of the hands present probably the most common and the most vivid of the cutaneous expressions of the disease. They are, as also the other affected surfaces, usually symmetrically involved, the eruptive symptoms when fully developed spreading evenly from the radial to the ulnar side of the hands, sparing the palms and nails (Fig. 3). In but a few cases, those seen by us in the South, have the palms been invaded by extension from the back of the hands. Raymond asserted categorically that the dorsum of the distal phalanx is never attacked, and this even when the region named has not been protected by the position assumed in grasping tools employed by the laborer in the open fields. These statements, however, have been negatived by numerous observations in every large experience.

Dr. Watson points to a characteristic extension of the pellagrous eruption on the hands to the flexor surface, beginning on the radial border, and reaching toward the ulnar by an oblique line forming an irregularly outlined triangular patch, its base at the radius, its apex near the ulnocarpal articulation.

The dorsa of the feet, when exposed equally with the hands,

are similarly affected. The eruption covers the area from the distal phalanges of the toes to the malleoli, as a rule, sparing the heel.

In exceptional cases, departures from the type are striking. The "pellagrous boot" we have seen chiefly in Southern patients; the eruptive symptoms spreading somewhat unevenly from the foot to the upper third of the leg, displayed, as a rule, more abundantly in front than behind. In many cases we have seen distinct

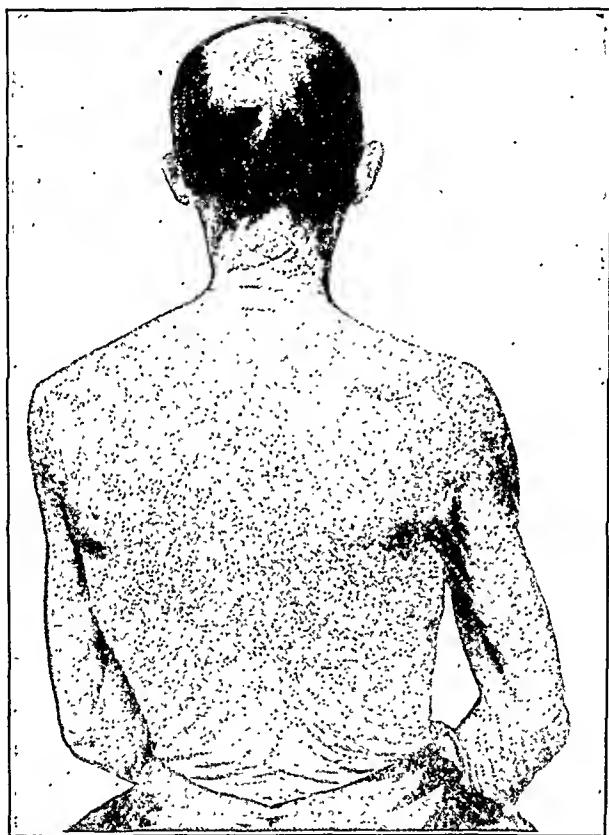


FIG. 4.—Pellagrous erythema, universal. (Courtesy of Dr. Miller.)

involvement of the knees when the legs were scarcely invaded. The same is true of the upper extremities, the entire forearm becoming the seat of the eruption, with distinct limitation to the region exposed to the light, showing a line of demarcation at the wrist, the elbows being very distinctly involved, with circumscribed borders. Again, tongue-shaped prolongations may spread from the elbows downward as far as the middle of the forearm. Where the clothing worn by the day laborer has a V-shaped opening in front and behind (as is seen in some of the Egyptian sufferers),

there is a corresponding localization of the eruption, the erythema spreading downward in a triangular patch, its base above both in front and behind. Similarly produced are the irregular areas of involved skin occasionally perceptible over one or both shoulders. The genital region in both sexes is at times attacked, notably the scrotum in men and, more often, the vulva in women. Miller has reported an instance of pellagra universalis (Fig. 4). Cases have been recorded, however, in which, after the exposure of the entirely nude body, the face, hands, and feet only have been involved (Neusser).

The hue of the exanthem differs according to the color scheme of the subject and the length of time during which it has existed. At first the color is a dull red, which has been likened to the appearance of the skin after a common sunburn; yet it is rare that the pinkish hue produced by the rays of the sun in the skin of a blond subject is precisely imitated. The pellagrous erythema at the outset, generally fading temporarily under pressure, is more reddish than pinkish, displayed at times with discrete macules which speedily fuse and produce, on the backs of the hands, for example, a uniformly smooth, reddened, and distinctly outlined area, suggesting, when the cuffs have definitely limited the efflorescence above, the appearance of a glove covering the back of the hand. In the milder cases the macular lesions may fade without producing the "mask" effect; more commonly the eruption persists to a complete involvement of the areas exposed to the light. As the evolution of the erythema advances, the color deepens, refuses to disappear under pressure, and at its height attains a reddish-brown, chocolate, or plum-colored shade, described as "livid bluish," a tint at times suggesting that of sepia. The first eruptive symptoms may disappear in a fortnight with epidermic exfoliation in light flakes, leaving behind a pigmentation differing according to the severity of the precedent engorgement.

The skin thus affected is tense, swollen, and the seat of burning rather than of pruritic sensations. The surface is very rarely scratched. In the dark races, especially the negro, the color of the eruption may take on a grayish hue, with deepening of the normal pigment of the part.

Cases exhibiting vesicular and bullous lesions, in both the northern and southern portions of this country, are popularly termed "wet" (Fig. 5), as contrasted with the "dry" form described above. In these instances vesicles and blebs develop, often with large elevations of the epidermis over chambered sero-pus, followed by desiccation, crusting, and rhagades. These are decidedly the rarer exhibitions of the exanthem, and are believed to be concomitants of the most serious phases of the systemic disorder.

In most of the first attacks the eruptive phenomena fade in a fortnight, leaving the skin pigmented, roughened, and, in the case

of many of the poorer class not under hygienic management, begrimed with dirt.

Many, indeed, of the American patients have a recrudescence of the exanthem in the autumn, some under our observation suffering even from repeated attacks in one season; while the type cases of Italian writers undergo a relighting of the morbid process in the

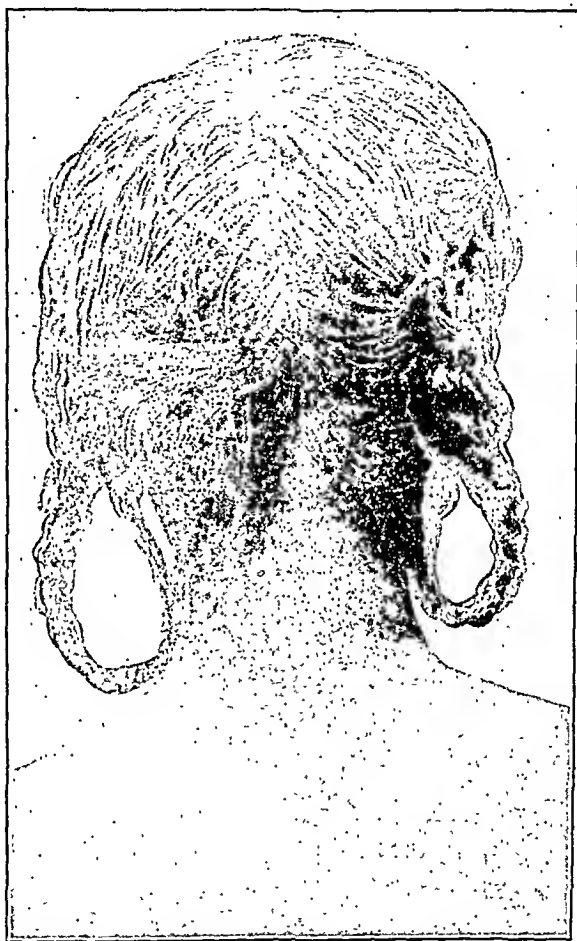


FIG. 5.—Pellagrous erythema of the neck, moist type. (Courtesy of Dr. Zeller.)

skin, only at the succeeding season of spring (second stage), when possibly, without the production of as vivid an exanthem as at the first, the skin again becomes dull reddish in hue, is more deeply infiltrated, and, when the exacerbation passes, in cases in which the hands are involved, leaves these organs covered with a seamed, corded, rugous, and irregularly roughened epidermis, which has given pellagra its distinctive title.

In cases in which a vesico-bullous efflorescence occurs, the picture presented on the back of the hands, after bursting and crusting



FIG. 7.—Atrophy of the skin of the back of the hand succeeding pellagrous erythema. (Reproduced through the courtesy of Prof. Ludwig Merk, of Innsbruck.)





have been accomplished, is that of the skin which has been the seat of artificial vesication (Fig. 6). A granulating surface where the epiderm has been removed becomes covered with a new and tender horny layer, which presents itself with limits furnished by the ragged, partly adherent, and slightly loosened fringes of dirt-colored skin. In cases in which no fluid has been effused, the affected surface scales in larger or smaller flakes of loosened epithelium. After one or more attacks of pellagrous erythema, the skin atrophies, leaving in the site of the exanthem a thinned, cicatriform, parchment-like integument, this last often irregularly altered, the thinning

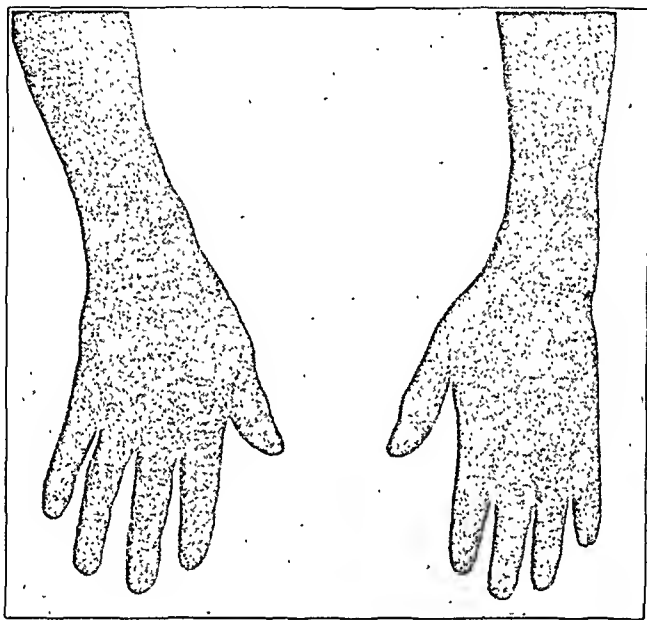


FIG. 6.—Pellagrous erythema of the hands, bullous type. (Courtesy of Dr. Zeller.)

showing occasionally in striae parallel with the long axis of the hand, rarely as a definitely bordered scar, such as follows ulceration of the integument (Fig. 7).

In severe cases, however (one such was shown us in Columbia), after the onset of the exanthem, ulceration occurs on the backs of the hands. In a few of these the sheaths of the tendons have been exposed. When recovery has ensued, the scarring has not resulted in attachments to the tendinous sheaths.

In several patients seen by us in Bartonville, the pellagrous erythema was complicated with very marked ecchymoses. These were visible in deeply empurpled patches of otherwise typical areas of erythema. In a negro woman, shown us by Dr. Babcock, in Columbia, an odd-looking, lunar-shaped, ecchymotic area, its concave border upward, was visible beneath each lower eyelid.

The severity of the roughening of the skin of the hands and other regions displayed in the severest types of cases (rugous folds interspersed with furrows of atrophied, scaling, or deeply pigmented and discolored integument) can readily be distinguished in the body after death. This feature is in contrast with some of the severe dermatoses of the body which, post mortem, are scarcely demonstrable.

The pellagrous exanthem is of the order of the toxic erythemas in general, a local expression of a systemic disorder. That its manifestations are awakened by the action of the actinic rays of light upon the exposed surfaces of the skin is incontestable. That this is not solely a reactive result of exposure to such rays is equally clear. Reference is made above to erythema exsudativum, as it is called chiefly in Europe, a disorder due to a systemic infection, yet accompanied by local eruptive phenomena, not invariably, but often, limited to the hands. Arsenical pigmentations and verrucæ of the palms and soles are illustrations of a chemical action not always, but often, having a similar localization. The familiar syphilides of the palms and soles exemplify the localization of symptoms in a disorder which often is exhibited by lesions elsewhere situated, but which for years may be betrayed solely by manual or pedal symptoms. Explanations of these facts are not difficult. The hands and feet are organs not only situated at the greatest distance from the circulatory centres, but also far more exposed than other parts of the body to the accidents of contact with the external world. Dr. Michell called our attention to the frequent congestions of the hands of insane patients, due to their habits.

Many subjects of melancholia and other mental disorders can be seen in the buildings and about the grounds of asylums with their hands depending listlessly by the side and unmoved for hours at a time.

Though the systemic condition is no less essential, the rays of the sun are actually requisite for the production of pellagrous erythema. The result is comparable to that obtained when a chemical reagent is added to a solution containing a suspected ingredient, and which at once demonstrates the presence of the latter by causing a precipitate.

Experiments have been made by exposure of the hands to the sunlight when the organs were partially protected with gloves fenestrated so as to admit the rays to the skin to definite regions only. In these instances the erythema has been limited to the parts exposed to light through the fenestrations. That the sunlight in pellagrous erythema is effective merely because of the weakened resistance of the tissues in the class of patients chiefly liable to the disease is disproved in a photograph shown by Dr. Zeller. The patient, a woman, had paralysis of one hand. The

paralyzed hand was spared; the back of the other hand became the seat of a characteristic rash.

It is especially noteworthy that, given the general toxemia, even feeble exposures to solar light suffice to determine the exanthem. Prolonged exposures are not essential to the awakening of the local efflorescence. This fact was emphasized by the condition of the hands of a patient shown us in the Elgin Asylum. The patient, a woman, suffering from melancholic dementia, had been bedridden for years, and occupied a room in common with another insane woman, also pellagrous. The first patient occupied a bed at the farther extreme corner of an apartment lighted by a single window. The only light accessible for a long period prior to the advent of the pellagrous disorder was furnished by this one window. Yet the hands of this woman, who was suffering from an incoercible diarrhoea, exhibited a perfectly classical picture of the pellagrous "glove," the deep staining of the skin of the hand reaching the wrist, where it was sharply delimited by the cuff of the sleeve worn in the bed. This woman soon after died, and was found, post mortem, to have had fatty degeneration of the liver and other organs.

An interesting control of this fact is furnished in the experience of the Inspector of Insane Hospitals for the State of New York, Dr. Russell, who has examined thirty thousand insane patients under his supervision, presumably as much exposed to sunlight as any of those in Illinois or South Carolina. None of this large number was recognized as pellagrous.<sup>2</sup>

The differential diagnosis of pellagrous erythema is not obscure. Majocchi, in describing the conditions of the hands resembling the pellagrous skin, occurring in patients who are the subjects of chronic alcoholism, declares that the "pellagrous glove," with its distinct limitation at the wrist, is usually wanting; the affection is less often symmetrical; too often extends in an irregular line along the lower forearm; lasts for a longer time; and the ensuing pigmentation is of later occurrence.

The several manifestations of erythema multiforme which affect the hands, both papular and bullous, certainly exhibit different shades of color. The peculiar crimson quality of the isolated papules and tubercles seen in that affection on the backs of the fingers and the hands almost never fuses into a sheet of puffy redness in that situation, never presents the picture, viewed from the back, of the gloved hand. Weeping eczemas of the back of the hand could not be mistaken for a pellagrous exanthem, seeing the invariably irregular contour of the affected patch, its special itchiness, its peculiar color, and persistent ooze on slight provocation.

It may be unsafe at this time to assume that the shade of color seen in a type case of pellagrous erythema, observed at the date

<sup>2</sup> Personal communication.

of full evolution of the eruption, is unique and characteristic. But one is tempted to such a conclusion after close inspection of a hundred patients. In a typical case, to the eye trained in nice discrimination of shades of color, the special hue of the pellagrous skin is unmistakable. There is a quality of reddish-brown in the uniformly stained and puffy integument which confirms the diagnosis. Certainly, the pre-variolous rashes in a menstruating woman, the toxic erythema of Asiatic cholera, and the burns, whether of the first or second degree, produced by the action of solar light, of steam, and of heated water, in the white race, exhibit no such characteristic tint.

In what has been described as the second stage of pellagra, the nervous and psychical disturbances first betrayed in the vertigo, headache, backache, tremor, and lassitude experienced in the early period of the disease, become more pronounced. A profound mental depression, often resulting in settled melancholia, occasionally alternating with periods of psychic excitability, occurs in most instances, and may be followed by stupor and hallucinations. Only a small proportion of patients observed abroad become insane. The symptoms of what has been termed "true pellagrous insanity" differ so widely that at this point the student of the disease is confronted with a confused multiplicity of symptoms, contrasting with the uniformity of the cutaneous lesions to which attention has been directed. While the body-weight in these cases decreases, the patient often refusing food, he frequently becomes the victim of hallucinations, delusions respecting guilt, persecution, and attempts upon his life. In rare cases epileptiform and even cataleptic seizures occur. Seeing that pellagra occurs among the tuberculous, the syphilitic, the subjects of tabes and tabo-paralysis, of dementia paralytica, of uncinariasis, of amœbic dysentery, of bilharzia disease, and of other affections, it is not surprising that a distinct and characteristic imprint of the pellagrous poison upon the brain and nervous system does not seem to have been clearly determined.

Scheube and other writers have called attention to the tendency of demented pellagrous patients to commit suicide by drowning (hydromania), for the reason, it is surmised, that the subjects of the hallucinations common in this disorder are impelled to the act by a vague desire to cool the burning mouth or the irritated skin. But a comparison of statistics leads to the conviction that there should be some reserve in accepting these conclusions. From the admirable *Dunning Report of Pellagra in Italy*, it appears that in that country but 10 per cent. of pellagrous patients become insane. Now, the deaths from pellagra per 100,000 inhabitants in Lombardy, which may be called the home of pellagra, amounted in 1907 to a total of 10.4. In Veveto, which suffered more than the other provinces, the percentage of deaths from pellagra in 100,000 of

inhabitants for the same year was 18.4, the highest obtaining in any of the provinces for the year named. Granting that but one in ten of these patients died insane, and supposing that of these even one in three managed to commit suicide by drowning, the deaths from that cause would only equal the number (0.6) of suicides by drowning in each 100,000 of sane and insane inhabitants of the entire United States for the same year, the number for each year from 1900 to 1907 being practically the same.

Even allowing for the possibility that some victims of pellagra not insane ended life by drowning, and, further, assuming that other patients under proper surveillance made futile attempts at self-destruction, the figures yet speak for themselves.

The gastro-intestinal symptoms of pellagra, as has been seen, occur in all stages of the disorder, and not rarely constitute its most intractable feature. Often the characteristic diarrhœa, equally severe day and night, accompanied by meteorism and pyrosis, develops simultaneously with the erythema. The redness of the tongue, whether of the mild or of the "bald" variety, which results from an exfoliation of the buccal epithelium, in some cases is associated with profuse salivation. In one of the patients, a colored woman, shown us at Columbia, the saliva flowed freely from the lips. Dr. Babcock, in this connection, pointed out in some of the patients a peculiar, pinpoint-sized, blackish or bluish-black pigmentation occurring at the apex of some of the filiform papillæ of the tongue, an observation confirmed by Watson in a number of negro patients (Lavinder's "stipple tongue"). In some cases these conditions of the buccal membrane have coincided with similar changes in the rectal and vaginal mucosa. In many instances patients exhibit the severest symptoms of dysentery, with bloody evacuations. In the terminal stages of pellagra, peristalsis of the intestine may cease. In exceptional cases there is constipation rather than diarrhœa. Nesbit, reporting the results of his stomach analyses in 10 cases, found 4 showing marked diminution of acidity of the gastric juice, and 5 with excess of mucus. There did not seem to be any change in motility.

The so-called third, or terminal, stage of pellagra has been described as typhus pellagrosus. The condition is one in which there is merely grave accentuation of the symptoms declared in the other artificially classified stages of the disease. No typhus, as that term is now understood, is present, and *Bacillus typhosus* (Eberth) is not demonstrable. The patient may have a symptomatic fever, declared for the first time during the progress of the disease. He is usually profoundly prostrated; there is extreme weakness from the intestinal flux which has preceded, with emaciation and stupor, or mild delirium. The diarrhœa at the last may intermit.

A striking feature of this terminal stage is opisthotonos, the patient lying upon the bed with the head forcibly extended, the

general musculature in a state of great rigidity. Oddly enough, this is one of the few constant symptoms of the disease in its final stage. Coincidentally, there is extreme tenderness of the loins and back, less directly over the spinal region than over the points where the spinal nerves make exit from the vertebral canal, a few inches from the spines on either side. This was exceedingly conspicuous in one of Dr. Watson's patients shown us, to whom reference has been made, a negro lad in the last stages of pellagra who, attempting to stand and walk, accomplished these acts with a rigidity of the muscles of the trunk and extremities simulating the symptoms seen in dengue fever.

When investigating the neurological phenomena of pellagra, Dr. Bassoe, of our commission, was able to make a careful examination, extending through the greater part of two days, of a group of selected patients in the Peoria State Hospital.

Practically all of these patients were in an advanced state of dementia, utterly precluding inquiry into their subjective symptoms, especially those relating to sensation. Inasmuch as all the subjects were reported to have been insane for years before the appearance of symptoms suggestive of pellagra, they could not be suffering from true pellagrous insanity, and their mental state was not of special significance in connection with this inquiry. In almost all the cases, examination, not merely of sensation, but of all functions requiring coöperation on the part of the patient, being out of the question, we were limited to testing the reflexes, and even this in many instances was difficult. The chief aim was to reach some conclusion respecting the frequency of signs of degeneration in the cord or peripheral nerves.

Fourteen men and eleven women were examined. Four men and eight women presented sufficiently marked increase of the tendon-reflexes to suggest the probability of some degree of degeneration of the pyramidal tracts. One of these men and four of the women had a more or less constant Babinski sign. One woman and one man presented signs of degeneration of the posterior columns alone, as most of the tendon-reflexes were lost; others were greatly reduced; the woman also was extremely ataxic. One woman probably had a combined degeneration of the pyramidal and posterior tracts, as there was loss of tendon-reflexes, with an inconstant Babinski sign on one side. No instance of local or multiple neuritis was observed. We could find no reason to believe that any of the cases with changes in the reflexes were instances of combined pellagra and tabes, spinal syphilis, multiple sclerosis, or other independent organic nervous disease. The following are examples of the three groups encountered:

A. *Probable Pyramidal Tract Degeneration.* Case I.—Demented male epileptic, aged thirty-seven years, admitted April, 1902; previously at a poor farm and another State hospital. Insane for nineteen years. Diarrhoea and erythema of the hands during the

past summer. The hospital record mentions increased tendon-reflexes and positive Babinski sign on August 31, 1909. Examination on October 10 revealed increase of all tendon-reflexes without clonus; inconstant Babinski and Oppenheim signs; pupils react to light. There is slight swaying in Romberg's position, but the patient walks well and the heel-knee test is as good as can be expected in a demented subject. A note was made on October 31 that he had had stomatitis and diarrhoea for several weeks, and lost forty pounds in weight.

*B. Posterior Column Degeneration.* Case II.—An elderly demented woman developed characteristic skin lesions in August, 1909. Ataxia is so marked that she cannot walk or stand alone. The wrist, elbow, knee, and ankle-reflexes are lost. No Babinski sign. No involuntaries. Pupils normal. Characteristic erythema of the hands and face when examined on October 10.

*C. Combined Degeneration.* Case III.—A woman, aged fifty years, was admitted in November, 1908, with a history of having been insane for fourteen months. On admission she was fairly well nourished and the tendon-reflexes were normal. The psychosis was melancholia of involution. On August 27, the wrist- and elbow-reflexes were recorded as normal; the knee-reflexes as increased. No Babinski sign at that time. On October 10 she was emaciated, with severe stomatitis and diarrhoea. The wrist-jerks and the left elbow-jerks were absent; the right elbow-jerk, weak. Knee- and ankle-jerks absent. Inconstant Babinski sign on the right side; normal flexor response on the left side. The pupils reacted rather sluggishly to light. She died on the following day. No necropsy. It seems probable that the pyramidal tracts were first involved, causing increased knee-reflexes. Later, the posterior columns degenerated sufficiently to abolish nearly all of the tendon-reflexes.

Nine patients affected with typical pellagra were selected at this time by Dr. Davis, of our commission, for blood examination from the abundant material available. They were fairly representative cases, and should present in a general way the blood picture as it appears in the disease as it existed in Peoria.

#### BLOOD EXAMINATION IN CASES OF PELLAGRA.

Blood cultures.	Erythrocytes.	Hemoglobin.	Color index.	Leukocytes.	Polynuclears.	Small mono-nuclears.	Large mono-nuclears.	Eosinophiles.	Basophiles.
Negative	4,514,000	86	0.95	7,600	79.6	12.3	6.4	1.2	0.5
"	2,816,000	71	1.20	24,000	74.6	13.7	11.7	0	0
"	4,736,000	86	0.90	20,600	67.3	19.1	19.6	0	0
"	4,616,000	77	0.84	15,500	59.6	25.4	14.5	0.5	0
"	4,040,000	86	1.05	14,600	70.0	23.1	6.4	0.5	0
"	3,760,000	78	1.04	13,500	77.5	11.4	10.6	0	0.5
"	3,390,000	76	1.12	13,050	65.5	28.0	6.6	0	0
"	4,040,000	77	0.95	13,100	65.8	9.2	24.2	0.8	0
"	3,464,000	77	1.10	14,300	74.1	20.0	5.5	0	0.4
Average	3,930,700	79.3	1.01	15,140	69.77	18.02	11.72	0.33	0.16



Blood cultures were made, using for media ascites broth and plates of agar. The blood, obtained by withdrawing 5 to 10 c.c. from a vein at the elbow, was distributed into large tubes of broth, to which ascitic fluid had been added in the proportion 4 to 1, and into melted agar tubes, which were at once poured into plates. The tubes and plates were then placed under aerobic and anaerobic conditions and examined from time to time for growth. In all cases the results were negative. Generally, the cases showed a slight grade of anemia. The red cells varied from 2,816,000 (Case II) to 4,736,000 (Case III). The hemoglobin (the Dare instrument was used in all cases) varied from 71 per cent. to 86 per cent. The color-index ranged from 0.84 to 1.2, five of the cases having an index a trifle over 1. In Case II the index was sufficiently high to suggest the type of pernicious anemia. In this case the red cells were counted twice and two hemoglobin determinations made, with substantially the same results. The average index of the nine cases is 1.01.

In connection with these results, the fact should be noted that nearly all of these were bedridden patients, in whom the peripheral circulation was sluggish. This would tend to give higher readings, and due allowance should be made for this condition.

The number of white corpuscles in this series of cases is strikingly uniform. The lowest count was 7600 (Case I), and the highest was 24,000 (Case II). In most of the cases the number ranged from 13,000 to 15,000. Differentiation did not give marked variations from the normal. The polynuclear cells varied from 59.6 per cent. to 79.6 per cent., the average in the 9 cases being 69.7 per cent. The small mononuclears ranged from 9.2 per cent. to 28 per cent., averaging 18.02 per cent., and the large mononuclears varied from 5.5 per cent. to 24.2 per cent., averaging 11.72 per cent. This is somewhat in excess of the normal number of large mononuclears, which is usually given as 5 to 6 per cent. The increase, as shown by the table, occurred in 5 of the cases, the other 4 giving normal percentages of these cells. It is especially noticeable in Case VIII. Basophiles were rare, as were also the eosinophiles. In only 4 of the cases were the latter found, and then usually only after counting several hundred leukocytes. Over a thousand leukocytes were counted in some of the cases without finding a single eosinophile. Especial attention was given to these cells, for the reason that an eosinophilia is often found in various skin diseases, and also in conditions in which the intestinal tract is infested by animal parasites. Inasmuch as intestinal symptoms were common in these cases,<sup>3</sup> in addition to the skin lesions, this point seems noteworthy. Myelocytes were not found in any of the

<sup>3</sup> Postmortem examination in Cases III, VI, and VII of this series revealed inflammatory or ulcerative lesions in the intestinal tract. In these cases also amœbæ were reported to be common in the stools.

cases, nor were nucleated red cells encountered. The erythrocytes in stained preparations gave no evidence of polychromatophilia or poikilocytosis, and basophilic degeneration was not observed.

Compared with the observations made by others on pellagra cases, the results here recorded agree in that a mild grade of anemia was found, and also in the fact that many of the cases gave an increase in the large mononuclear cells. According to Lavinder and others, a leukocytosis is not usually found, except in association with secondary complications, which not infrequently occur, especially in the later stages of the disease. Postmortem examination of some of these patients disclosed, for example, lesions of the intestine which may have been responsible for the leukocytosis observed. Such lesions, however, are not rare. If they constitute an essential part of the pathology, the fact has not been definitely established.

These results are practically those reported by other observers at the Pellagra Conference. For the most part (there was but one exception) the eosinophiles were unmistakably few and the mononuclears numerous, the increase being in cases noteworthy. Microorganisms, save in the exceptional hematozoa cases, were absent. Howard Fox, after an examination of 30 cases in Columbia by the Noguchi modification of the Wassermann test, found that in pellagra there was no positive reaction. When weak reactions were obtained, they were without difficulty distinguishable from those secured in syphilis and lepra.

The ocular symptoms in pellagra have been studied in America by Seiler, Watson, and Welton, of Peoria, who kindly showed us the record of his findings, the pellagrous conditions of the eye being compared with carefully made control observations. Pupillary changes with bilateral or monolateral mydriasis, conjunctivitis, retinitis, inflammation of the optic nerve, and especially chorioiditis, are not rare, the grade of the eye changes in general, as might be expected, presenting severity corresponding with the general symptoms. In one of the patients examined by us photophobia was pronounced. In a small percentage of the fifty-five patients examined by Welton, there was paralysis of the ocular muscles. In none were eye-symptoms recognized as pathognomonic of pellagra.

Though pellagra is not an inherited disease, its occurrence in children is noted by many writers on the subject. Pellagrous women often abort; others bring into the world infants who, when living in pellagrous districts, speedily develop the malady, the offspring being not rarely stunted, as well as deformed.

The fruit of pathological research in pellagra serves to illustrate in a conspicuous manner the marked absence of any constancy in the changes wrought by the disease. The earlier cutaneous alterations are similar to those found in the exudative erythemas, while in the terminal stages the microscopic picture is practically

that presented in the senile skin. Depending on the type of the inflammatory reaction and the stage of the process when the examination is made, the histological changes vary from those found in simple erythema to those seen in marked bullous dermatitis. Still later, atrophy of the papillæ and sclerosis of the vessels of the corium with hyperpigmentation and hyperkeratinization of the epidermis are found, the latter identical with those found in the senile skin. The parenchymatous neuritis of cutaneous nerves recorded by Déjerine has not been confirmed by other observers.

Scheube, Sandwith, and Tuzcek agree that in many cases there is pigmentation of many of the viscera, wasting of the muscular and fatty tissues (especially atrophy of the muscular coats of the intestine), brown atrophy of the heart, atheroma of the larger vessels, hepatic enlargement, splenic shrinkage, fragility of the ribs (Lombroso), cirrhotic changes in the kidneys, and, as respects the nervous system, either no perceptible changes, or in the brain, cord, and meninges evidences of chronic inflammation, subarachnoid hemorrhages, cerebral atrophy, and symmetrical sclerosis of the posterior columns, especially those of Goll. Occasionally the posterolateral columns in the dorsal region are similarly involved. Marie believes that these cells are, in general, primarily involved.

Harris ascribes the variability in the recognized organic lesions to the extreme chronicity of the disease and to the further fact that most postmortem observations have been made in subjects who were for a long time victims of the malady. His observations include, besides those enumerated above, atrophy of the pancreas, softening of the cord, signs of Belmondo's "meningo-myelitis acuta," with marked degenerative changes in the myelin-sheaths of the nerves, of the nerve cells of the gray substance, and of the ganglia. Peripheral nerve changes have not been recorded.

The following is, in brief abstract, the record of an autopsy made by us in October, 1909, on one of the Bartonville subjects. It illustrates the inconstancy of postmortem results in some of these cases. The negative findings are not enumerated:

W. E., aged forty-two years, developed pellagra early in August, 1909. The cutaneous and other symptoms subsided, but recurred four days prior to the date of the autopsy. Recent symptoms included severe abdominal pains, diarrhœa, and a scaling dermatitis of the hands.

*Anatomical Diagnosis.* Moderate grade of dermatitis of the dorsum of the hands; right serofibrinous pleuritis; healed tuberculosis of the pleura; chronic suppurative cholecystitis; chronic ascending cholangitis; cholelithiasis; multiple abscesses of the liver, with rupture into the peritoneal cavity; acute suppurative peritonitis; acute splenitis; acute nephritis; icterus; pigmented Peyer's patches; acute purulent tracheitis and bronchitis; fibrous adhesions about the gall-bladder and in the lesser peritoneal cavity; obstruc-

tion of the common bile duct. *Bacteriology*: From the bile, peritoneal fluid, heart's blood, pericardial and pleural fluids, *Bacillus coli communis* was obtained in pure culture.

Nichols found a very high percentage of protozoal infections of the colon in the pellagra patients examined by him in the Peoria State Hospital, and at the Pellagra Conference exhibited sections of intestine with unmistakable ulceration of the mucosa, the result of amœbic dysentery. Schreiber, however, in three patients who were not amœbic, recognized, post mortem, superficial ulcerations of the mucosa of the colon.

A survey of the records of pellagra in this country suggests an inquiry which seems to have attracted but little attention up to the present time, as to whether the majority of patients in America were first insane and later became pellagrins, or whether they were first pellagrous and later, either as a complication or a consequence of the affliction, became insane. This question is somewhat intricately bound up with another, namely, for how long a time has pellagra actually existed in the United States?

Some of the physicians of the South are disposed to believe that pellagra has claimed its victims in this country for twenty-five years. Williams and Mobley cite cases which seem to have been well-marked instances of pellagra, occurring twelve and ten years ago. Watson exhibited to us in Columbia a negro boy, twelve years of age, whose symptoms were of the most pronounced and classical type—cutaneous, digestive, nervous, and ocular. He had suffered for five years, and for two years continuously with cutaneous lesions (pellagrous "gloves," "boots," Casal's "neck-band," etc.). Several superintendents of asylums are reperusing letters and reports sent in the past by members of families to whom either the bodies of dead or restored patients had been returned, complaining of maltreatment of these individuals by attendants through scalding the hands and other parts of the body—instances of what is now believed to have been pellagra. Zeller cites one such case in which a nurse had been dismissed in disgrace, but was restored to duty after the facts were more fully understood.

On the other hand, the evidence that many inmates of asylums were insane before they became pellagrous seems conclusive. These are often ex-inmates of workhouses, pauper asylums of different sorts, debilitated long before their admission to the institution where they were recognized as pellagrous, their lives rounding out a full measure of misery and physical degeneration. The mouths of many are in the worst possible condition. One cannot conceive of a class of subjects more fit for the invasion of the special poison of pellagra. The fact that the insane may become pellagrous is by no means newly attested. Brière de Boismont, Billot, and others describe in detail pellagra as "manifested during the course

of mental disease." Baillarger cites cases in which pellagra appeared some time after the admission of insane patients to the asylums in Turin.

An important point in favor of the conclusion that the insane of some of our asylums have recently become pellagrous is to be found in the character of the skin symptoms. It is within bounds to declare that the most of the cases seen by us showed face, hand, and neck symptoms belonging to the early rather than the late pellagrous stages, as evidenced by the vividness of the erythema and the absence of the atrophic sequels of the invasion of the skin.

It is noteworthy in this connection that the same question respecting the prior existence of pellagra was asked when the malady first appeared and spread in Italy to such an extent as to arouse the attention of the physicians of that country. It has, however, been generally accepted that there could have been few cases observed by medical men before the middle of the eighteenth century, as the symptoms of the disease were then scarcely enumerated in literature.

The cause of pellagra is unknown. It would exceed the compass of this article to set forth the arguments pro and con of the "zeïsts" and "antizeïsts," namely, of those who do and of those who do not believe that the ingestion of maize is responsible for the disease. On the one hand stands Sir Patrick Manson, who categorically disputes the position that either the nutritive ingredients of sound corn, or toxin which it may contain, or even fungi or bacteria (*Bacillus maidis*, *Ustilago maydis*, *Bacillus pellagræ*, *Penicillium glaucum*, *Aspergillus flavescens*, *fumigatus*, *varians*, etc.) accidentally developed on the grain are, any of them, effective. It is true that one of his arguments is weakened today by his citation of the United States as a corn-eating and pellagra-free community. It is certain that those who have never consumed corn have had pellagra. It is equally certain that experimental consumption of spoiled corn by man has not resulted in the development of the disease. Further, it is undemonstrated that cattle suffering from "blind staggers" and other disorders, as well as chickens dwarfed after a diet of "pellagrozein," as Lombroso termed it, were victims of pellagra.

On the other hand, to the mass of evidence in favor of some connection between the consumption of maize and pellagra collected by skilled observers and scientific men in various parts of the world, a conservative judgment cannot fail to assign value. The National Pellagra Conference held in Columbia (1909) assumed a judicious position by declaring: "That while corn is in no way connected with pellagra, evidences of the relation between the use of spoiled corn and the prevalence of pellagra seem so apparent that we advise continued and systematic study of the subject, and, in the meantime, we commend to corn-growers the great importance of fully maturing corn on the stalk before cutting the same."

Recognizing, however, a fact of importance in this connection, namely, that pellagra has occurred in persons living on a diet consisting largely of durra (Indian millet, Guinea corn), it is probable that a much wider scope must be allowed for the play of the special toxin effective in the production of the disease, if its etiological factor is ever demonstrated to be closely related to a cereal diet.

The full report by Dunning on Pellagra in Italy would seem to furnish overwhelming support to the proposition that maize is responsible for pellagra, were it not for the evidence it presents of efforts on an enormous scale put forth by the Italian Government, not merely in the direction of excluding maize, and especially spoiled maize, from the dietary of their peasantry, but also in the line of a wide improvement in the general hygienic environment and food of the people. The admittedly impoverished condition of the great mass of sufferers points unmistakably to the predisposing causes of the malady. The setting of these aside in large measure has naturally produced a noteworthy change in the statistics of the disease in Italy. How far these can be cited as arguments in favor of the zeïstic origin of pellagra is questionable. The indisputable facts in this connection are the occurrence of the disease as an endemic; its practical limitation within definite geographical limits; its involvement of men, women, and children, at all ages, but especially of adults between the third and fifth decades of life; and that its victims everywhere belong to the class of those whose resistance is weakened by poverty and such of its attendant ills as insufficient and improper food, exposure, and unremitting toil.

The brilliant successes in the management of pellagra have been secured by prophylaxis. Amelioration of the environment, food, and mental state of pellagrous patients living in pellagrous districts has worked surprising results.

The Italian campaign against pellagra has been conducted by enactment of laws providing for inspection and condemnation of suspected food imports; by requiring registration of all pellagrous cases; by the establishment of pellagrological commissions, such as that recently authorized by the Illinois Legislature;<sup>4</sup> by founding pellagrosarios, institutions for the care of the sick; by distributing proper food to destitute families; by erecting "economic kitchens" and rural bakeries, where food of proper quality is supplied at a low price; by appointing commissions (*Cattedre ambulanti*) for instruction and encouragement in improved methods of agriculture; and by providing public desiccating plants for drying maize, and public storehouses for its preservation. An elaborate system of

<sup>4</sup> The Governor of Illinois has appointed a commission to report upon pellagra in the Charitable Institutions of the State, consisting of the following-named gentlemen: Dr. Frank Billings, Chicago; Dr. J. L. Greene, Springfield; Dr. Geo. W. Webster, Chicago; Dr. H. S. Grindley, Urbana; Dr. Howard T. Ricketts, Chicago; Dr. Oliver S. Ormsby, Chicago; Dr. H. Douglas Singer, Hospital; and Dr. W. J. McNeal, Urbana.

public education has also been put in operation by lectures and distribution of pamphlets. The happy results are worthy of study as well by the economist as by the physician.

Compared with these, the fruits of medication of those who are infected are scarcely worth naming. Arsenic by the mouth and by hypodermatic injection, atoxyl administered by both methods, quinine, strychnine, iron, have been both praised and adjudged of little value. Drs. Cole and Winthrop, employing transfusion with the blood of both cured pellagrous and non-pellagrous subjects, seem to have secured satisfactory results in a few cases. Today the best accepted treatment of the disease is that which is indicated in individual cases by the symptoms presented, always having in view the imperative demand for improved nutrition.

The extent of the prevalence of pellagra in the United States is set forth in the observations of Lavinder, who has had opportunities for the observation of the disease in all parts of this country. The first cases were reported by Dr. Gray, of New York, and Dr. Tyler, of Massachusetts, at the meeting of Asylum Physicians, held in Washington, D. C., in 1863 and 1864. Before these dates there had been reports of isolated cases occurring near Halifax, N. S. I was present at the meeting of the American Dermatological Association, in 1902, when Dr. Samuel Sherwell, of Brooklyn, reported two cases occurring in Italian sailors found pellagrous after entering the port of New York. Lavinder's list of those of the States where pellagra is believed to have occurred includes the names of thirteen, mostly Southern, to which Illinois and other States have since been added, making a total believed to be sixteen. Most of the cases reported are in public institutions of one kind or another, chiefly asylums for the insane. At the date of the appearance of Lavinder's leaflet it was believed that a total of one thousand cases had been recorded. The number has since increased. Dr. Kerr estimates that there were five thousand pellagrins in the United States in the year 1909.

Respecting the prognosis of pellagra, the percentage of mortality among American patients seems to be nearly 35 per cent. of those affected. Unfortunately, the larger number of fatal cases has occurred among the insane presumably affected with the disorder after admission to the institutions reporting the fatality. Statistics of pellagra in its terminal stages in this country, where the course of the disease from onset to conclusion was wholly and purely due to the pellagrous poison, are not available. Randolph, basing his conclusions upon the Florida cases, believes that about one in every four or five patients recovers. Of the series of cases studied by Siler, 22 per cent. died, 10 per cent. were failing, and 17 per cent. improving at the date of his report. In a personal communication received from Dr. Zeller since the adjournment of the Conference, he reports the death of several patients observed by us when per-

mitted to make the observations recorded in this article. Most authors agree as to the curability of the disease in its earliest manifestations, chiefly by the aid of the generous regimen suggested above. Fritz, director of the Pellagrosario at Inzago, in a long experience, has seen but two complete cures of fully developed cases.

Physicians in all parts of the United States are now somewhat anxiously regarding the possibilities of the future respecting the progress of pellagra in this country. The history of the disease in the past points with emphasis to the fact that in countries where it has once attacked the population it recurs with somewhat alarming regularity, save when such elaborate measures of repression have been adopted as those briefly outlined above in connection with the campaign against pellagra in Italy. What will be the issue of the oncoming spring and summer when, according to the common mode of the malady, its recrudescence in a severe form might be anticipated? It is probable that there may be during the year 1910 a considerable increase in the number of cases reported.

But he has poorly comprehended the economic equations of our national resources who looks to see pellagra work such havoc in this country as among the smitten peasantry in the provinces of Bergamo, Brescia, and Venetia. It has been aptly said of the poor of America that they do not know what poverty is. Incredible as it may sound to those unfamiliar with the fact, a large number of the applicants to public charities, in the Northern States at least, are food-poisoned by sheer glut. They are not even strangers to the gout.

The lessons of pellagra are writ too large to be neglected in any wide measure by an intelligent people. Its cause, as yet undetermined, will be revealed; its prophylaxis is already understood; it certainly will be relegated to that path whither uncinariasis has been consigned, and along which yellow fever and tuberculosis are already disappearing.

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## HIGH CALORIC DIET IN TYPHOID FEVER.

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THE present death rate of typhoid fever is very low, notwithstanding many serious complications which are possible. But there is much to be gained in comfort to the patient. The classical three weeks cannot be aborted, but the prospect of an average lower temperature and pulse rate with lessened meteorism, toxemia, and delirium is very alluring. By due regard for the dietary, this end can be achieved in all but a few severe cases.

My object is to consider this subject from the standpoint of the physiologist and at the same time take account of the altered conditions in the intestinal tract and the deviations from normal metabolism. If the subject is approached with a spirit of fairness and with a desire to examine closely the more exact experimental evidence, one can hardly escape the conclusion that the use of milk and various "peptone" preparations is based on prejudice and precedent, and has little else to commend it. To recommend indefinite quantities of foodstuffs without inquiry into their chemical architecture and the needs of the patient is inexact and unscientific. Shaffer<sup>1</sup> has estimated that the typhoid fever patient rarely receives more than 50 per cent. of food necessary to supply dynamic needs. This usually contains at least three times more nitrogen in proportion than would be advisable to allow a healthy individual. Naturally the balance of the dynamic needs must be met by the body tissue with consequent loss of weight and increasing weakness.

The use of milk—plain, fermented, or digested—is strongly entrenched in American practice, and it is difficult to obtain consideration of other foodstuffs. The argument that milk is "easily digested" loses force in direct proportion to the number of curds in the stools and the degree of meteorism. If sufficient is given to meet dynamic needs, the bulk is almost prohibitive. It neither protects against nitrogen loss (if that is desirable) nor does the chemical structure of the casein molecule permit of its rational use.

The favorable results obtained with Seibert's<sup>2</sup> soup diet led to this article. He does not use milk. The relative amounts of protein, fat, and carbohydrate are difficult to estimate, but there is a commendable increase in energy producing elements. The cases reported are sufficiently numerous to draw satisfactory conclusions concerning the death rate. But most convincing to the judicial observer is the frequent absence of necessity for baths and

<sup>1</sup> Jour. Amer. Med. Assoc., 1908, li, 974.

<sup>2</sup> Medical Record, June 20, 1908.

stimulation, and the absence of those symptoms which make the life of the typhoid fever patient miserable.

**THE DIGESTIVE SECRETIONS IN FEVER.** In general, typhoid fever is a disease characterized by ulceration of Peyer's patches—the organs of protein assimilation—diffuse catarrh of the intestinal mucosa, and by a *Bacillus typhosus* bacteremia. Experimental medicine has shown that the glandular secretions of the digestive tract are diminished or altered. Jawein says that the total quantity of salivary juice is less than normal; it is often acid, and ptyalin is absent. Dry mouth and sordes are always present.

Kraus<sup>3</sup> has this to say of the gastric secretions: "The amount of HCl is so small that the affinity of the food is not satisfied. Organic acids contained in the food or derived from it by fermentation preponderate in the chyme. Von Noorden obtained, *together with numerous negative results*, distinct evidences of HCl during the high fever of erysipelas and scarlet fever, provided large amounts of salt and pepper were added to the meat taken." According to Sticker and Zweifel, the power of absorption is diminished, but the motor functions seem to be undisturbed.

The hepatic functions in typhoid fever are also altered. Post-mortem degenerative changes are found and acute yellow atrophy may follow intense toxemia. There is a diminution in the quantity of the bile (Bidder and Schmidt), it is more viscid, and contains an abnormal amount of mucus (Pisenti). Naturally there exists no evidence as to the integrity of the pancreatic secretion or the succus entericus. That these digestive juices, in common with others, are diminished in quantity and altered in quality, particularly in typhoid fever, is the natural and justifiable assumption. There is an admitted 10 to 12 per cent. decrease in the digestive capacity of the typhoid fever patient for all classes of foodstuffs (von Hoesslin). With the above facts drawn from precise observation before us, are we justified in believing that 10 to 12 per cent. covers the amount lost?

It is my purpose to omit discussion as to the power of the fever patient to digest and assimilate fat and carbohydrate. There is not the necessity for the use of fat, notwithstanding its high caloric value. Its tendency to produce digestive symptoms is a positive contra-indication. As to starches and sugars the question will hardly arise. Von Leyden and Klemperer, von Hoesslin, Folin, and others believe that it is normal within the above percentage, and the evidence on which their conclusions is based is seemingly conclusive. On the other hand, protein assimilation in fever will demand some detailed attention, for it is important to know whether

<sup>3</sup> Where references are not given in detail, they may be found either in von Noorden's "Metabolism and Practical Medicine," Lusk's "Science of Nutrition," or in the papers definitely indicated. Such sources of information have been freely summarized with a view to presenting the subject as cogently as possible.

the benefits from its use overshadow the disadvantages. The present view that digestion and assimilation of protein is normal within 10 per cent. rests on the accuracy of the nitrogen balance as an experimental procedure. Does nitrogen which has disappeared en route through the fevered digestive tract mean normal utilization?

**PROTEIN ASSIMILATION IN FEVER.** Accepting Chittenden's standards for the purpose, a normal man ingesting daily 60 grams of protein (about 11.5 grams of nitrogen) and sufficient fat and carbohydrate to yield 2000 to 3000 calories, will pass 2 grams (or less) of nitrogen in the feces. The difference—all but one gram, more or less—will be eliminated in the urine. This is assuming that his work is light, and that other factors, such as external and internal temperature, etc., are medium, normal, and constant.<sup>4</sup> It is not possible to differentiate the sources of fecal nitrogen in a given case. According to Voit, who tied off intestinal loops in dogs, most fecal material is true excrement from the walls of the intestines or glands emptying therein. Strassburger<sup>5</sup> estimated that one gram of nitrogen in the normal stool is contained in the bodies of bacteria, which may have arisen from food or secretion nitrogen. There is also nitrogen to be found in desquamated cells, carbon nuclei fractions resulting from bacterial activity and other minor sources. Further, in typhoid fever there may be blood and reparative serum exudates which have survived the destructive influences above mentioned. So economical is the organism in the use of foodstuffs that there is very little nitrogen residuum from intake. It is probable that fecal nitrogen may vary in its distribution at different times and in different individuals, and that the distribution may be materially altered within a short period.

An increase in protein intake does not cause an increase in the nitrogen of the feces until the capacity for assimilation is far exceeded. The first effect is increased nitrogen exchange, and the evidences appear in the urine. As soon as it reaches the lower limit of heat requirements in the starving man, oxidation and heat elimination increase, and the thermo-regulating mechanism is called into play. This is the effect of the specific dynamic action of protein as demonstrated by Rubner. The second effect of the overuse of meat is usually increased intestinal putrefaction, with increase of its products in the urine and sometimes in the feces. It is only during recovery from disease, growth, and prolonged muscular exercise that the body is able to retain any quantity of nitrogen by increased protein feeding.

Approximately 82 per cent. of the urinary nitrogen is eliminated in the form of urea. This substance has no single source. A

<sup>4</sup> Rieder found that a man on a non-nitrogen diet passed 0.54 to 0.87 gram of nitrogen in the feces daily. These values are about 0.5 gram greater than Müller found in the starving Cetti. This is the minimal value of secretion nitrogen not reabsorbed.

<sup>5</sup> "Die Faeces des Menschen."

portion is derived from the liver and in part represents unused residual ammonia fractions arising as required alterations in molecular form take place in the change from the food to body proteins. A portion is derived directly from food proteins by simple hydrolytic splitting, such as may occur after the ingestion of arginin. A portion is the end-product of cellular metabolism. Urinary creatinin is exogenous and endogenous, the latter, according to Folin, being a measure of cellular metabolism. The same is true of xanthin bases. Sulphuric and glycuronic esters are products of intestinal putrefaction.<sup>6</sup>

The urinary nitrogen of the fever patient shows alteration in distribution. The total amount is increased proportionately to the intake. The quantity of endogenous purins increases with the fever (Mandel), and proportional to the whole nitrogen output. Ammonia in combination with organic acids always increases, and often at the expense of urea ammonia. This ammonia excretion shows a total weight from 2 to 6 grams as against 0.7 gram in health. The creatinin nitrogen on a creatinin-free diet shows a ratio to total nitrogen of 0.2 to 4.5 as against 5 to 7 in health (von Noorden). The excretion of indican may be increased by eight or ten times over the health maximum. In severe infections the distribution of nitrogen may be so altered as to resemble the toxemia of pregnancy (Ewing).

**KIDNEY CAPACITY IN FEVER.** The reasons thus far advanced to show the limitations of the nitrogen balance more particularly involve problems of metabolism. There are some others which involve the activity of special organs. The quantitative elimination of nitrogen by the kidneys varies in a most unaccountable manner, following to some extent the cyclic elimination of health, but without the precise periodicity. The variations, however, furnish considerable leeway for error, unless the period of observation is prolonged. Epicritical elimination of nitrogen, following the termination of an infective process seems to point in the same direction.<sup>7</sup> The possibility that nitrogen may be retained in the form of excrementitious products, secondary to the irritation of infection must be admitted, and may under these circumstances be the equivalent of latent uremia.

**NITROGEN EXCRETION BY THE SKIN DURING FEVER.** Nitrogen is excreted in the perspiration, the whole amounting from 0.2 to 0.66 gram daily (Atwater and Benedict). Increase in nitrogen elimination usually follows increase in the quantity of sweat, as the

<sup>6</sup> The nitrogen in these compounds is small. The significance lies in the fact that they represent a definite amount of protein, disintegrated by extradigestive processes, which also may be represented in the ammonia output.

<sup>7</sup> Epicritical elimination of nitrogen has been explained on different grounds. As an example of retained nitrogen from non-elimination, Schondorff found that after feeding a dog an abundance of meat, there was 40 grams nitrogen accumulation in the tissues "in the form of water free extractives and 20 grams of urea nitrogen."

result of muscular exercise. The external temperature and humidity also have their effect. Argutinski found that he excreted 750 mg. perspiration nitrogen in the summer and less than a third of that amount in autumn. These results can hardly be applied to an infective process, because circulatory disturbances are an inevitable accompaniment. The contraction of peripheral arterioles not only inhibits conduction and radiation, leading to retention and fever, but the supply of sweat-producing materials to the skin is diminished. There is, therefore, a diminution in refrigeration. By measurement, the evaporation of water from the skin during fever is normal, but observations on this point do not seem to be conclusive. Admitted as true, the effort of the organism to lose heat through evaporation neutralizes the contraction of arterioles from infection. Proportionate to the rise in temperature, the amount of perspiration is therefore diminished. From a clinical standpoint, this view is hardly satisfactory. One can scarcely watch the periodic and irregular drenching of bedclothes without wondering whether nature has overcome the tendency of the infection to curtail evaporation, and thus the laws for the irregular excretion of urinary nitrogen become operative for the skin. If uncalculated in the nitrogen exchange, the uppermost limit of sweat excretion during muscular activity would lead to an error of 12 or 15 per cent. on Chittenden's diet.

**BACTERIAL DISINTEGRATION OF PROTEIN.** F. Müller suggested that the amount of body protein destroyed by bacteria was sufficient to take into account, but there has never been general acceptance of this view. Of more importance are bacterial processes in the intestine during fever, and especially typhoid. The withdrawal of digestive juices and delay in digestion of protein is an opportunity which intestinal bacteria do not neglect. This is shown by the large excretion of urinary aromatic sulphates, the meteorism, and foul stools. We are unacquainted with bacterial processes in the intestine during typhoid fever. We know nothing of possible powers which *Bacillus typhosus*, acting alone or in symbiotic activity with *Bacillus coli* or anaërobics, may have in disintegrating food-stuffs and thereby producing a toxemia independent of but augmenting the intoxication of the disease. The amount of protein lost to the organism in this manner cannot be estimated, but it must be considerable on a high protein diet.

**CONCLUSION.** It is not forcing the conclusion to say that a daily nitrogen balance does not necessarily indicate proper digestion, absorption, and utilization of protein in the fever patient. "It is by no means certain that the amount of nitrogen retained is a measure or the equivalent to accumulation of body albumin" (von Noorden). Only as the nitrogen of the food becomes an integral part of cell life (Hoffmeister's stabile protein) is it servicable to the organism. Potentially, it may become of service in the form



of labile protein. With a healthy organism and by suitable food—a minimum of protein and maximum of carbohydrate and fat—the nitrogen exchange would tend to diminish to a point where it would coincide with true nitrogen metabolism. In practice this point is rarely reached, and, if possible, would be of doubtful value (Meltzer). These facts should make us extremely skeptical concerning the utilization of protein by the fever-infected organism—especially in typhoid fever.

**METABOLISM DURING FEVER.** It is of prime importance, in deciding on a dietary for fever patients, to recognize certain altered metabolic processes and thereby adjust the supply to the requirement.

*The Causation of Fever During Infection.* Increased oxidation brought about through the action of toxins on thermo-regulating centres in the central nervous system is usually given as the cause of fever. Inquiry into the respiratory quotient, heat elimination, and the condition of the circulation bear out this conception only with modification. Von Noorden measured the daily calorie output of a typhoid patient weighing 48 kilograms, the fever ranging about 38.5° C., and found that he eliminated 1200 calories, or 25 per kilogram. The patient preserved his weight on a diet rather rich in protein. No relation has been established between the degree of pyrexia and perceptible alterations in the respiratory quotient. There may be an increase in oxidation processes, but in a large majority of cases the respiratory quotient and caloric output remain normal.<sup>8</sup> The character of ingested food seems to have more influence than any other factor.

The maintenance of body temperature during muscular work and increased oxidation depends on loss of heat through conduction and radiation, and secondly by evaporation of water, mainly through the skin and to a less extent through the expired air. Conduction and radiation are limited by circulatory changes in infective fever. This action begins as soon as the absorption of toxins commences by causing a general constriction of ultimate arterioles. Heat production and heat outgo become equal after the first thirty-six hours, with the body temperature at a higher level.

It seems probable that some degree of pyrexia in typhoid fever may be accounted for by oxidation processes in the intestine due to bacterial activity, especially in cases in which the food content is favorable for such action. Thermogenic bacteria are common inhabitants of the bowel (Macfadyen).<sup>9</sup>

*Increased Protein Destruction in Fever.* An increased destruction of cellular protein which shows itself in urinary nitrogen is always noted in infective fever. This loss is attributable to the

<sup>8</sup> Increased oxidation is always noted during the initial rise of temperature.

<sup>9</sup> Jour. Path. and Bact., 1895, iii, 87. (Full references to French literature.)

cause of the fever or the infective process, and the loss does not account for the increased pyrexia. In a case observed by von Leyden and Klemperer, the diet contained 25.1 grams of nitrogen in twenty-four hours and the excreta contained 31.5 grams, of which 29.6 grams appeared in the urine. On the observed day the patient received a total of 1732 calories, and the highest temperature was 40.2° C. There was a nitrogen loss of 6.4 grams. The cause of such losses may be found in two directions: (1) Destruction due to the rise of body temperature. This is shown best by the loss of nitrogen in animals subjected to a high temperature. Voit found that by artificially raising the temperature of a fasting dog to 40° for a period of twelve hours, there was an increase in nitrogen elimination of 37 per cent. above the normal. There was no toxic element to obscure the picture. (2) Nitrogen loss due to the virulence with which the toxins attack body tissue. This varies with the character of the infection. According to Ehrlich, the labile protein molecule and the toxin molecule both contain haptophore groups, and the mechanism of attachment to cellular protein is the same. During infection, cellular protein exhibits greater affinity for toxins than labile (food) protein. If this were not so, immunity processes would be seriously inhibited. Therefore, in severe infection, with abundance of toxins in the circulating blood, cellular activity results in augmented nitrogen output. Regeneration is possible only as the intoxication decreases and attachment of nutrition nitrogen supercedes that of toxin nitrogen. It will be possible to maintain cell equilibrium of nitrogen only when side-chains available for nutrition are equal in number to those combining with intermediary bodies. If the former exceed the latter as the infective process subsides, cell regeneration takes place and the effect is retention of nitrogen in the form of stabile protein.

*Metabolism of Fats and Carbohydrates in Fever.* In pyrexia the glycogen of the liver disappears and that of the muscles increases. This migration is probably accounted for by the need of the cells for combustible material. The burning of body fat is proportional to the burning of protein, and plays its part in the weight decrease. After absorption the behavior of carbohydrates is not materially different from that in health.

*The Acidosis of Pyrexia.* An increase in the output of urinary ammonia (in combination with acid) has been noted. This may reach as high as 6 grams (normal 0.7 gram). The three acetone bodies have been isolated, and feeding starch does not always cause them to disappear. Von Noorden was inclined to attribute their appearance to inanition and lack of nourishment. They certainly indicate perversions in oxidation power. It is interesting to note in this connection that Herter has isolated small amounts of acetone from cultures of mixed fecal bacteria. Since it has been shown that the acidosis of diabetes is not dependent on bacterial activity

in the intestine, too little importance has been attached to a possible connection. Kraus is of the opinion that determination of the acidity of the urine is of little value. There is a type of acidosis which reveals itself by hyperacid urine, decrease in salivary alkalinity, and possible hyperchlorhydria. Some symptoms of this type accompany fever. Whether the acidity can be referred to destruction of body or food protein<sup>10</sup> cannot be said.

*The Internal Organs in Fever.* While in many instances the functional capacity of an organ can be conjectured by postmortem changes, urinary evidences of decrease in renal function are too well understood to need more than passing mention. It must be granted that these organs bear the brunt of the infection and are most susceptible to its influence. The hepatic changes also have been mentioned. As to the condition of the glands having internal secretion, but little is known. It would be a most curious confirmation of clinical observation if it could be shown that vasomotor dilatation so characteristic of certain infections depended on failure of the adrenal gland.

*The Specific Dynamic Action of Foodstuffs.* Many years ago, Rubner recommended that the excessive use of protein in infective fever was contra-indicated by its specific dynamic action. This is best illustrated by experiment on a starving dog. The heat produced was observed to rise 42 to 46 per cent. after consumption of 2000 grams of meat. At the height of digestion, the increase was still greater, sometimes attaining 90 per cent. The effect passed off at the close of the tenth hour. As long as the protein consumption remains high, the energy transformation remains high. According to Rubner, for every 1 per cent. addition to the protein of the food, there is an increase in the consumption of energy on a pure meat diet of from 2 to 2.5 per cent.<sup>11</sup> The constant deposit of protein continually raises the heat production in the organism until a point is reached when no more protein is added to the body.<sup>12</sup> This is the point of nitrogen equilibrium, and when the sparing action of fats and carbohydrates is utilized, the point is quickly attained. It is evident that on a purely protein diet the dynamic needs cannot be met, the same conditions obtaining in a less degree by a use of a relative excess of protein. The only exception to this rule is when the intake of protein is less than the dynamic needs of the starving organism at rest. This increase in energy con-

<sup>10</sup> The proportion of bases to acids in the protein molecule averages 25 to 35. Mann's Chemistry of Proteins.

<sup>11</sup> It is usually calculated that 20 per cent. increase in the dynamic value of food for fever patients should be allowed over that of the resting individual. It would be interesting if it should transpire that this resulted solely from protein consumption.

<sup>12</sup> We are not at liberty to use the terms "heat equilibrium" and "nitrogen equilibrium" as synonymous terms. There may be loss of weight with nitrogen retention. There may be heat equilibrium with loss of nitrogen. To assume that an individual is in heat equilibrium because there is a nitrogen balance or gain would not be allowable until weight had been maintained for a long period.

sumption is manifested by increases in oxidation and consequently is manifested in the respiratory quotient. This specific dynamic factor which averages in the case of protein 30.9 per cent. has been found to be 12.7 per cent. for fat and 5.8 per cent. for sugar, carbohydrates in general falling between the last two figures. With respect to fats and carbohydrates, this increase in energy consumption has been referred to increased activity of digestive glands, but for proteins it is attributable to the specific action which protein has upon oxidation processes in the cell.<sup>13</sup> Magnus-Levy has shown that the effect is not produced by meat extractives, while Lusk, basing his opinion on Mandel's work, is inclined to attribute it to the uric acid group.

Svensen's work in general, shows that the same principles apply to the typhoid fever patient, finding an increase in gaseous exchange after meals.

**SOURCES OF CORPORATE ENERGY.** The caloric values of protein, carbohydrate, and fat are well understood. The point to be especially elucidated involves the source of energy in protein. The amount is relatively small, and there is good reason to believe that it can be referred to its carbohydrate content or to carbohydrate derivatives. Pavy has shown that nearly all proteins contain a carbohydrate group preformed in the molecule. This may attain 10 per cent. It is quite possible that the transformation of sugar from protein may determine the available source of energy in protein. Lusk, also, has shown that 52.5 per cent. of the energy contained in meat protein may be liberated under certain circumstances as dextrose in the organism, and this directly used by the cells. Protein as a source of energy is, therefore, not as economical as carbohydrate or fats, the organism being unable to maintain heat production by its use without the assistance of more easily combustible foodstuffs.

**THE STANDARD FEVER DIET.** The ideal fever diet should consist of such foodstuffs as will meet the dynamic needs of the organism, and prevent excessive loss of weight until natural immunity processes terminate the disease. Its specific dynamic action should be as small as possible, and the end-products of metabolism should be such as to be capable of elimination without additional strain to those organs. If, by reason of digestive limitations, the food is subjected to bacterial influences, the end-products of such alteration should present the minimum of toxicity. Of considerable importance is the danger of increasing the relative acidosis through improper food, or possibly augmenting the fever through excessive use of purins.

The objections to protein as a foodstuff for the typhoid fever patient having been pointed out, it remains to show that, as compared with probable damage, very little good follows its use. To maintain

<sup>13</sup> To illustrate this point, an exact comparison between the patient with fever and an individual subjected to high external temperature is allowable.

the body in nitrogen equilibrium does not prove that protein reaches the cell and becomes a part of intracellular life. In fever there are many influences which may turn it aside from its normal pathway. Nitrogen metabolism in pyrexia cannot be altered to the normal as long as the infective process continues, the toxic destruction of the cell strictly limiting regeneration even with a large protein intake. In the latter event the nitrogen exchange is raised, and the toxic destruction of cellular protein continues. Nitrogen loss in infectious diseases is the inevitable consequence of the disease, and while not desirable if it can be prevented, still it is yet to be shown that its loss is *per se* objectionable.<sup>14</sup> In any event, if the sparing action of fats and carbohydrates is used to the fullest extent compatible with appetite and digestive capacity, it is probable that this deprivation of protein food will not figure in the death rate.

Voit has shown that carbohydrate may spare the loss of body albumin from overheating by subjecting a starving dog (the same dog!) whose temperature had been raised to 41° C. for a period of twelve hours and noting that 40 grams of cane sugar protected against nitrogen loss. The toxic element was not present in this experiment, and the loss due to pyrexia alone was compensated. The starving nitrogenous metabolism can be reduced to one-third by the use of carbohydrates (Folin, Rubner). Siven maintained nitrogen balance in a man weighing 65 kilograms on 4 or 5 grams of nitrogen daily. Three and a half per cent. of the total caloric value of the food was in protein, the total being 2717. Chittenden found that nitrogen equilibrium could be maintained on a diet the caloric value of which was from 1500 to 1600. The first few days of Cetti's starvation shows that 13 per cent. of the total energy exchange was derived from protein and 87 per cent. (minus a small fraction derived from glycogen) from fat.

Von Noorden measured the daily caloric output of a number of fever patients. One suffering from typhoid fever yielded only 23 to 25 per kilogram of body weight. With lower values, weight was maintained by retention of water, as shown in many cases by developing œdema. Lower values sometimes were obtained in chronic fever, showing that prolonged intoxication of the cell was followed by low oxidizing power. This corresponds very well with the minimal caloric output of the resting healthy man as determined by Johanssen and others, the gaseous exchange remaining low. To this figure should be added sufficient to equalize the loss from the specific dynamic action of the foodstuff used, which in the case of carbohydrates and fats averages about 8 per cent. Von Leyden's estimate of caloric necessities for the bed-ridden patient, in diseases not involving metabolic perversions, was from 28 to 30 calories per kilogram.

<sup>14</sup> Concerning the condition of the cardiac muscle, the loss of tone in febrile states is probably due to overwork and toxic destruction, loss from pyrexia not entering as a factor.

These figures are given to furnish a suitable basis for computing the average needs of the patient suffering from typhoid fever. The advantage of arbitrarily establishing a standard for every patient is doubtful, even on a basis of weight. The practising physician recognizes that while the science of physics requires the use of precision instruments and takes cognizance of minute differences, it is not possible to proceed with such exactitude where vital forces are concerned. The totality of factors influencing cell activity is not yet apparent.

*The Use of Plain or Fermented Milk in Fever.* There are many disadvantages in the use of milk referable to its chemical composition. According to Dreschel, 9 per cent. of the nitrogen in casein can be separated directly by hydrolytic splitting into urea, this portion being of little service to the organism. The casein molecule contains 7 per cent. tyrosine and 1.5 per cent. tryptophane which under the influence of bacteria yield toxic phenol and indol compounds. It contains no glyocol.<sup>15</sup> To the chemist, casein is easily disintegrated, for it contains no peptones of the antigroup. Its use in practice demonstrates that when caseinogen is converted to casein by the action of lime salts, large curds form in the stomach and intestines, limiting the action of enzymes to the exterior surface, while bacterial processes continue on the interior. Sassetzky found that the loss of nitrogen on a milk diet in typhus ranged as high as 24 per cent. The absence of curds from the stools does not demonstrate the utilization of the casein molecule, sufficient time elapsing while traversing the gastro-intestinal tract to allow of bacterial disintegration. Impure, it adds infection to the intestinal contents.<sup>16</sup> It also furnishes excellent culture media for typhoid and other bacteria.

Rubner<sup>17</sup> says: "To cover a requirement of 2400 calories daily, 3410 grams of milk would be needed, which contains 140 grams protein!" This is more than twice the amount of protein contained in Chittenden's dietary for the normal men. It holds preformed in its molecule, carbon nuclei which are capable of great evil and does not contain those which are obviously of the most service.

*The Use of Alcohol as a Stimulant.* The caloric value of alcohol (72 grams equals 500 calories) makes it appear attractive as a stimulant. It is rarely if ever that the condition of the circulation calls for its use, viz., high peripheral pressure with failing cardiac tone. The opposite usually obtains. Recent work on the pharmacology of alcohol raises a very grave doubt as to whether it is ever beneficial.

<sup>15</sup> The chemical relationship between glycogen which disappears from the liver during fever and glyocol indicates that an abundance of the latter would be advantageous.

<sup>16</sup> The pediatricists recognize the value of bacteria-free food. Incidentally it might be added that cow's milk was originally intended for growing calves.

<sup>17</sup> Von Leyden's Handbuch, 1903, i, 132.

In closing, nothing better can be said than to quote the following spoken by Dr. Alexander Lambert<sup>18</sup> at a recent meeting of the American Medical Association: "I think if Dr. McCrea will leave out milk, he will be convinced that there is a better diet and a more generous one of rice, broth, sugar, butter, and a few crackers. It will open his eyes to the possibilities of a diminution in the toxicity of typhoid fever, a diminution of the delirium and meteorism in a majority of patients."

### SAMPLE DIET—TYPHOID FEVER.

Approximate values are based on the following data: Body weight, 60 kilograms; total caloric value, 2300; per kilogram body weight, 35 calories; distribution by weight, protein, 5.3 per cent.; carbohydrate, 55.5 per cent.; fat, 4.5 per cent. (Balance ash, water, and inedible refuse. This will yield 0.85 gram of nitrogen.)

Hour.	Material.	Weight. Grams	Approximate amount.	Percentage.			Calo- ries.
				Pro- tein.	Fat.	Carbo- hyd'te	
6 A.M.	Choice of: toast,	..	2 thin slices				
	Huntley and Palmer breakfast biscuit, or Zwiebach	35	5				
	Cup coffee, sugar	24	3	8.9	1.4	60.3	125
	Cream	8	2 heaping tea- spoonfuls	..	..	100.0	100
8 A.M.	Gruel, cream of wheat	60	1 dessertspoon- ful	2.4	17.6	4.5	35
	Oyster crackers	30	2 heaping table- spoonfuls	9.3	1.6	74.0	230
10 A.M.	Vegetable soup	250	Large handful	7.6	8.2	71.6	130
			8 ounces	*6.3	Negli- gible	43.9	190
12 M.	Baked potato	80	Size of orange	1.9	1.0	20.0	65
	Creamed after mashing	16	1 tablespoonful	2.4	17.6	4.5	35
	Butter	8	Size of a domino	1.0	80.8	..	60
	Hot weak tea, sugar	24	2 heaping tea- spoonfuls	..	..	100.0	100
2 P.M.	Toast	35	2 thin slices	8.9	1.4	60.3	125
	Tapioca pudding	60	2 tablespoonfuls	2.8	2.9	28.2	100
	Oyster crackers	30	Large handful	7.6	8.2	71.6	130
4 P.M.	Rice	100	.....	6.5	0.3	76.9	350
	Butter	8	Size of domino	1.0	80.8	..	60
	Sugar	24	2 heaping tea- spoonfuls	..	..	100.0	100
6 P.M.	Toast	35	2 thin slices	8.9	1.4	60.3	125
	Butter	8	Size of domino	1.0	80.8	..	60
	Sugar	12	1 heaping tea- spoonful	..	..	100.0	50
8 P.M.	Vegetable soup	250	8 ounces	6.3	Neg.	43.9	190
	Oyster crackers	30	Large handful	7.6	8.2	71.6	130

\* Percentage of solid material.

Weights of vegetables are those prior to cooking. Butter washed to remove free acid is preferred. All foods to be thoroughly cooked; four hours for vegetables other than potato.

*The Preparation of Vegetable Soup.* Sixty grams each of green or canned French peas, white dry beans, potato, rice, and noodles, and 15 grams of carrot are boiled in water at least four hours. Sufficient water should be added to make one liter—which is sufficient for four feedings. The whole yields 760 calories, of which 6.3 per cent. is protein, fat less than 0.2 per cent., and 43.9 per cent. is carbohydrate. When ready to use, stir up sediment and allow the patient to eat all (including noodles), with the exception of the pea and the bean skins. Onion may be added for flavor if desired.

*General Directions for Feeding.* The patient should be fed with a spoon by the nurse.

The food should remain in the mouth as long as convenient. Allow water between feedings, not at feedings.

Allowances or corrections are to be made for increase of nitrogen need during the first ten days and during convalescence. At the height of fever, if the patient cannot eat the full quantity, substitute isodynamic quantities of milk sugar. A relative decrease of weight should be reflected in the caloric value of the food on the basis of 4 kilograms of loss per week of disease.

## THE THERAPEUTIC USE OF BACTERIAL VACCINES.

WITH THE REPORT OF CASES.

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THIS study does not comprehend a discussion of the various theories of immunity, but is a description of the technique employed in making vaccines, with clinical observations on eight cases in which vaccines were employed.

**TECHNIQUE.** The technique followed was as simple as routine bacteriological work permitted. The preliminary step was the securing of cultures, either from the blood or pus, and determining the organism that produced the infection. In cases in which a general infection seemed to exist, blood cultures were first tried. If these were negative, then the organism was secured from the seat of local infection.

In cases of localized infection cultures from the pus as well as blood cultures were taken, in order that no unnecessary time might be lost. If blood cultures are positive, it is preferable to make the vaccine from that source, as one is then certain of the infecting organism; whereas cultures from pus are often mixed growths, and much valuable time is lost in plating for pure cultures. Besides



one is not sure which of the germs in the mixed culture is the organism doing the damage.

After the germ had been properly identified and a pure culture grown for eighteen to twenty-four hours on some solid media, such as plain or glycerin agar, the germs were scraped off and mixed with sterile normal salt solution, making an even emulsion. This emulsion was then standardized; that is, the number of germs per cubic centimeter of vaccine was determined by Wright's method. The emulsion was then placed in a hot box, kept at a uniform temperature of 65° C., and allowed to remain there for thirty minutes. After adding a capillary drop of lysol to each 10 c.c. of the emulsion and placing a sterile rubber cap over the neck of the bottle, the vaccine was placed in a refrigerator, and so kept except when using.

This technique is not difficult to master, and need not necessarily be confined to expert laboratory workers. The most difficult part of the process is the determination and isolation of the infecting germ. Care must be taken that spore-bearing germs are not present, as the temperature to which the vaccine is submitted will not kill spores. One may be assured that the vaccine is sterile by planting it on agar and incubating for twenty-four hours. If there is no growth, one is fairly sure that no spore forms or living organisms are present of the aerobic variety; anaerobes, such as tetanus and gas-producing bacilli should be searched for in smears; the clinical symptoms of the patient will suggest the necessity of anaerobic cultures.

The cases to be discussed are divided into two groups:

GROUP I. Those in which the organisms were demonstrated in the blood. Under this three forms of infection are presented: (a) Puerperal septicemia; organism, *Streptococcus*. (b) Septicemia following otitis media; organism, *Streptococcus*. (c) Septicemia accompanying ulcerative endocarditis; organism, *Staphylococcus pyogenes aureus*.

GROUP II. Those in which the organisms were not found in the blood. Under this five different infections are represented, general and local processes: (a) Appendicitis, complicated by pyemia and liver abscess; organism, *Bacillus mucosus capsulatus*. (b) Appendicitis, complicated by pyemia; organism, *Streptococcus*. (c) Puerperal fever, streptococcic endometritis. (d) Pelvic cellulitis, abscess in the cul-de-sac; organism, *Bacillus coli communis*. (e) Infection of the foot followed by cellulitis of the leg, complicated by erysipelas; organism, *Streptococcus*.

No attempt was made in these cases to limit the patient to vaccine treatment only. In every case the usual routine surgical or medical treatment was carried on, irrespective of the vaccine inoculations. It cannot, therefore, be said that the vaccine treatment was partly or entirely responsible for the cure. It was not the purpose of this paper to prove that vaccines only effected the cure, but rather to present the cases in such a manner as to encourage the use of vaccines

as an adjunct to medical and surgical procedures in certain types of infections which up until now have stubbornly resisted all curative measures.

GROUP I, Case I.—*Puerperal septicemia of forty days' duration; streptococci isolated from the blood; vaccine inoculations given; the temperature came to normal in two days; no further chills.*

Six weeks before admission the patient had been delivered at term of a healthy child. Fever set in immediately and ran a septic course. The patient had daily chills lasting from a half to one hour. During this six weeks the usual routine treatment was followed. She gradually lost her strength; but bedsores developed, the hemoglobin fell to 25 per cent. and the red cells to 1,000,000, and food could not be retained. There was considerable abdominal distention. In this seemingly hopeless condition vaccines were tried.

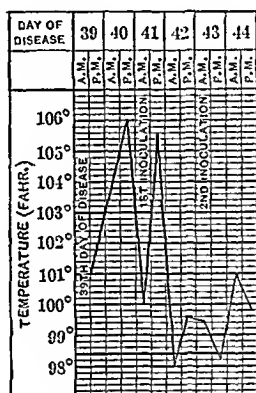


FIG. 1.—Temperature chart of Case I. Puerperal septicemia; streptococci isolated from the blood; autogenous vaccine used.

Streptococci having been isolated in pure culture from the blood, a vaccine was made, and 50,000,000 bacteria were inoculated on the fortieth day of septic fever. In two days the temperature had fallen to normal (Fig. 1), the chills stopped, and there was an immediate change for the better. The inoculations were repeated every third day, increasing 25,000,000 each dose, until six doses had been given. While the temperature had been lowered and the chills stopped, the patient's vitality was so depressed (the hemoglobin having fallen to 18 per cent.) that she would not respond to supportive measures, and died from inanition. In the light of more recent experience it would seem to me that the doses given were too large and may have contributed to the depression present.

GROUP I, Case II.—*Bacteremia following mastoid disease; streptococci isolated from the blood; treatment by autogenous vaccine and operation; recovery.*

A boy, aged seven years, came into St. Mary's Hospital with the following history: Two weeks previously he began to complain of

general malaise and headache, which lasted a full week. There was no chill; no nosebleed; but there was loss of weight, increasing weakness, and some night sweats. He was feverish at night. There was some earache in the right ear, but no discharge. (Later, the mother said the boy had been complaining of more or less earache for six weeks.) Physical examination showed a poorly nourished, fairly well-developed young boy. The left ear appeared normal. The right ear was reddened, and the drum seemed covered with a small amount of exudate; but was not bulging. The external auditory canal seemed smaller than the left. The chest, lungs, heart, abdomen, and extremities were negative. On admission the temperature was  $103.6^{\circ}$ ; pulse, 105; the respirations, 40. For the next ten days the temperature was of a septic type (Fig. 2), reaching as high as  $105.4^{\circ}$  on several afternoons and going to normal or subnormal in the forenoon. The pulse was rarely below 110, and several times as high as 128. On the second day after admission the right ear

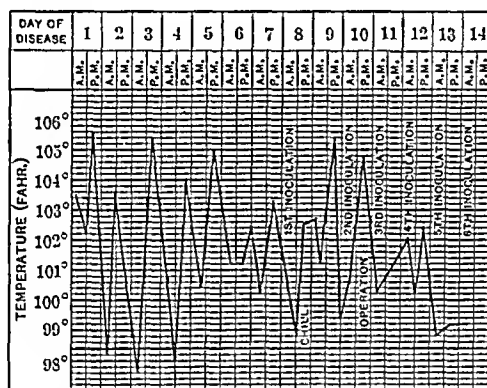


FIG. 2.—Temperature chart of Case II, showing the relation of the temperature to vaccine inoculations and operation. A case of mastoiditis; streptococci isolated from the blood.

drum was punctured and bloody serum escaped. Discharge during the next eight days was very scanty. On the fifth day the patient complained of pain in the left elbow and both knee-joints, which were slightly tender and swollen. On the sixth day after admission blood cultures were positive for streptococci. On same day tenderness was made out over the spleen and an endocardial murmur was heard; and two days later swelling was noticed in the subparotid region. The posterior lymph chain showed enlarged, discrete nodes, somewhat tender, but no fluctuation. The swelling in the parotid region rapidly increased, and operation for mastoiditis and sinus thrombosis was performed on the tenth day after admission. The mastoid was found but very little, if at all, involved, and on opening the sinus, a small amount of chocolate-colored material was removed. Cultures were taken, both from the mastoid cells and from the sinus, but were negative. Several glands from the posterior chain were removed



sion a blood culture was taken, and *Staphylococcus pyogenes aureus* was isolated, and a vaccine was made.

The leukocytes, on admission, were 18,000; the polymorphonuclears, 91 per cent.; large mononuclears, 4.5 per cent.; lymphocytes, 3 per cent.; eosinophiles, 0.8 per cent.; basophiles, 0.7 per cent. Fifteen days later the leukocytes were 50,000; the polymorphonuclears, 80 per cent.; large mononuclears, 14 per cent.; lymphocytes, 6 per cent. On the tenth day after admission the chest was aspirated and fluid obtained. Two days later signs of fluid in the pericardium were made out. The pericardium was aspirated, and over an ounce of clear fluid was obtained. During this period the heart action was very labored, and the pulse reached 132 per minute and was very feeble.

The first inoculation of vaccine was given on the seventh day after admission, and inoculations were given twice a week thereafter, until six had been given. The dosage was as follows:

First inoculation . . . . .	208,000,000
Second inoculation . . . . .	312,000,000
Third inoculation . . . . .	416,000,000
Fourth inoculation . . . . .	520,000,000
Fifth inoculation . . . . .	624,000,000
Sixth inoculation . . . . .	725,000,000

During the first two weeks of vaccine treatment the patient grew gradually worse. During the third week, however, his condition improved and his temperature gradually became normal (Fig. 3). His pulse, which had ranged between 110 and 130, became about 80, and the respirations, which had varied between 35 and 40, decreased to normal. During the third week of treatment his whole appearance changed and his strength steadily increased. After nearly four weeks of normal temperature, during which time marked improvement had taken place in his general condition, he contracted pneumonia and died.

GROUP II, Case IV.—*Pyemia following appendicitis; liver abscess; blood cultures negative; Bacillus mucosus capsulatus isolated from the pus on the fortieth day after operation; the use of vaccines made from this organism was followed by gradual fall of the temperature to normal and perfect recovery.*

J. E., aged forty-six years, came to operation for appendicitis after the usual symptoms. The appendix was found to be gangrenous. Behind the cecum was a small abscess. The appendix was removed, the abscess evacuated, and drainage inserted. The temperature did not rise above 101° on the three days following the operation, but chills, which had preceded the operation, continued and became more prolonged. The two weeks following operation showed a temperature septic in type and the patient's condition grew gradually worse. The wound was kept open and drainage seemed ample during this period. No enlarged liver could be made

out, though the patient became slightly jaundiced during the second week after operation, and occasionally complained of pain in the liver region. No further surgical measures seemed of use, and resort was had to intravenous injections of collargolum, and inunctions of Credé's ointment were given. These measures did not seem to affect favorably the course of the disease. Stock vaccines and antistreptococcic serum were used, with absolutely no results. The patient was in extremis. Blood cultures were entirely negative. A marked grade of secondary anemia was present, the red blood cells being 2,712,000. At this point an autogenous vaccine was made from cultures of *Bacillus mucosus capsulatus*, which was isolated from the pus of the appendix wound.

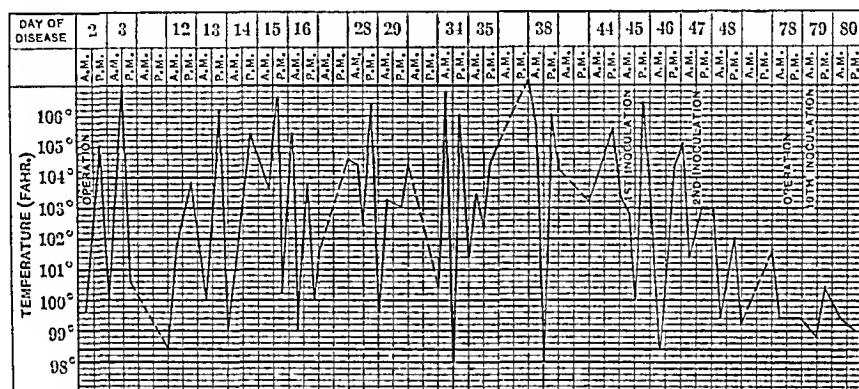


FIG. 4.—Temperature chart of Case IV, showing the temperature curve before and after inoculation. A case of pyemia with liver abscess following an appendix operation.

The first inoculation of the autogenous vaccine was made on the forty-fifth day after operation; thereafter two inoculations each week were made, with doses as follows:

First inoculation . . . . .	40,000,000
Second inoculation . . . . .	50,000,000
Third inoculation . . . . .	50,000,000
Fourth inoculation . . . . .	50,000,000
Fifth inoculation . . . . .	55,000,000
Sixth inoculation . . . . .	55,000,000
Seventh inoculation . . . . .	70,000,000
Eighth inoculation . . . . .	70,000,000
Ninth inoculation . . . . .	110,000,000
Tenth inoculation . . . . .	110,000,000
Eleventh inoculation . . . . .	110,000,000

Inoculations were then given weekly for a month at the same dosage, viz., 110,000,000.

After the first inoculation there was a slight fall in temperature (Fig. 4). After the second there was a decided fall. Chills, which had occurred regularly every day for forty-five days, ceased. The patient's general condition improved. The temperature remained between 99° and 102° for a month after inoculations began, during

which time signs of a liver abscess became evident. The abscess was opened and drained. *Bacillus mucosus capsulatus* was found in the pus from this abscess also. The temperature came gradually to normal after the abscess was opened, and the patient made a perfect recovery. Nearly one year later he reports himself in perfect health.

GROUP II, Case V.—*Postappendicular pyemia; abscess in the shoulder-joint; vaccine made from the pus; improvement after the second inoculation; perfect recovery.*

M. M., a woman, aged thirty years, was taken ill, eight days before admission, with the symptoms of appendicitis. At an operation performed immediately the appendix, perforated and gangrenous, was found enclosed in an abscess cavity, well walled off. Drainage was inserted and wound left open. The temperature for the first day after operation did not rise above

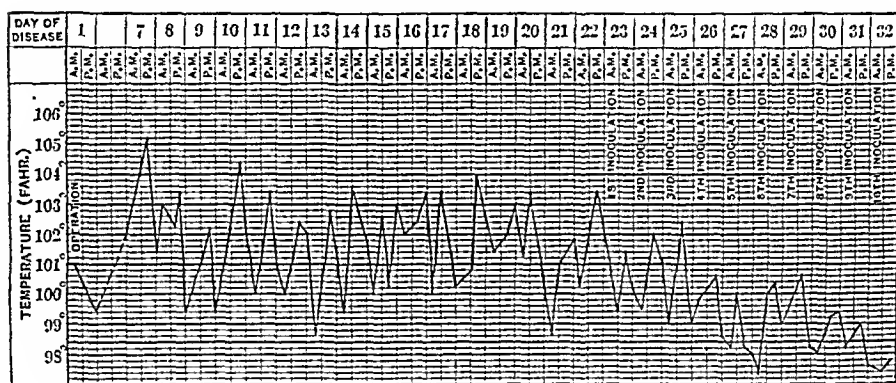


FIG. 5.—Temperature chart of Case V; postappendicular pyemia. The temperature curve before and after inoculations.

99.5°, but on the days following rose each afternoon and became septic in type. Five days after operation the wound was explored, but no pus pockets were made out; the abdomen was not rigid, and there were no signs of general peritonitis. On the ninth day after operation the left shoulder-joint was very painful, considerably swollen, and markedly tender. This continued until the seventeenth day after operation, when joint was aspirated and a seropurulent fluid obtained. Cultures from this fluid yielded a pure growth of streptococci. Several blood cultures were taken, none of which were positive. On the twentieth day after operation the right sterno-clavicular joint became swollen, tender, and slightly reddened, and the overlying tissue reddened. The leukocyte count on admission was 33,000; 89 per cent. polymorphonuclears; five days after admission, 33,300; 93 per cent. polynuclears.

On the twenty-second day after operation the first inoculation of autogenous streptococcic vaccine was given, the dose being 2,500,000. This was repeated daily until twelve inoculations had been given.

The temperature gradually came to normal (Fig. 5); her general condition improved from the first inoculation; the joint symptoms gradually disappeared, and the patient made a complete recovery. After the vaccine treatment was begun, all surgical and other medical measures were omitted. At the time inoculations were begun the patient was in a very critical condition.

GROUP II, Case VI.—*Puerperal fever, developing on the sixth day of the puerperium; blood culture negative; intra-uterine culture showed streptococci; stock streptococcic vaccine from a streptococcic septicemia was given, and the temperature came to normal, but rose on the second day; autogenous vaccine was then given, and the pulse, temperature, and respirations came to normal.*

A woman, aged thirty years, was delivered of a child at full term. For five days after delivery the temperature was normal; the uterus was contracted and the patient seemed to be doing well. On the sixth day the temperature suddenly rose to 105° in the morning

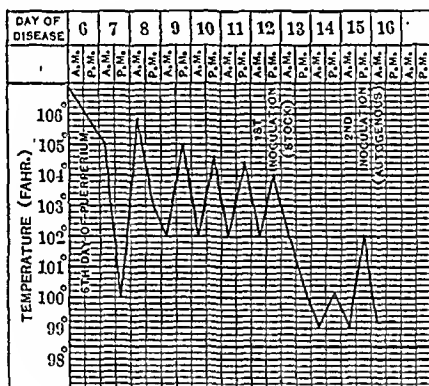


FIG. 6.—Temperature chart of Case VI; puerperal fever.

and dropped to normal in the afternoon. The next day it rose in the morning to 105.4° and fell in the afternoon (Fig. 6). The patient exhibited the usual symptoms of septic infection—rather drawn facies, rapid respiration, rapid pulse, extreme restlessness. On the sixth day of this septic infection blood cultures were taken, and no growth resulted. Cultures were taken at the same time from the uterine cavity. The cervix was patulous and considerable discharge was present. The intra-uterine cultures yielded a pure streptococcic growth, and a vaccine was made from this.

At the time the culture was taken, 50,000,000 stock streptococci were inoculated. (This strain of streptococcus was obtained from a blood culture taken from a previous case of puerperal septicemia.) The temperature came to normal the next day. Later it rose again, and on the third day the autogenous vaccine was inoculated, the dose being 100,000,000. The temperature again came to normal, being the twelfth day of the puerperium, and was followed by the



pulse and respiration. The patient had no further fever during the puerperium, and made a complete recovery.

GROUP II, Case VII.—*Pelvic abscess; Bacillus coli communis* was isolated from the pus; after many autogenous inoculations the temperature came to normal.

Two weeks before admission, after working hard, the patient began to flow, many clots coming away. This gradually increased and she became very weak. She had high fever at times, chills and sweats for three days preceding admission, and severe pain in the pelvis. Physical examination showed the abdomen to be slightly tender and rigid. The pelvis was tender on both sides, and over the

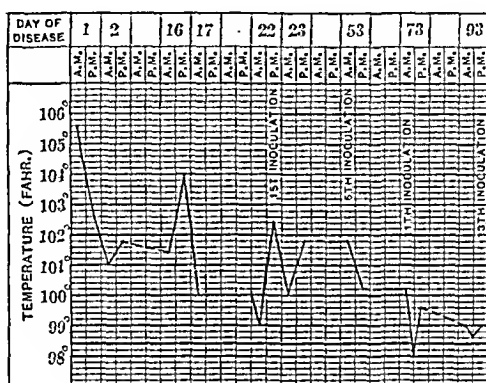


FIG. 7.—Temperature chart of Case VII, pelvic abscess. *Bacillus coli* infection.

uterus very rigid. The cervix was patulous. A large mass was made out filling the entire cul-de-sac, and very tender on palpation. An operation was made in the cul-de-sac and a large amount of pus evacuated. The fever continued, although drainage seemed ample.

The first inoculation was given on the twenty-second day of the disease. Thereafter inoculations were given twice a week, with dosage as follows:

First inoculation . . . . .	25,000,000
Second inoculation . . . . .	50,000,000
Third inoculation . . . . .	50,000,000
Fourth inoculation . . . . .	50,000,000
Fifth inoculation . . . . .	75,000,000
Sixth inoculation . . . . .	75,000,000
Seventh inoculation . . . . .	100,000,000
Eighth, ninth, tenth, eleventh inoculations . . . . .	100,000,000
Twelfth inoculation . . . . .	150,000,000
Thirteenth inoculation . . . . .	200,000,000

The temperature came gradually to normal and no further abscesses were formed in the pelvis (Fig. 7).

TYPE II, Case VIII.—*Infected foot, followed by cellulitis of the leg and later erysipelas; streptococci* were found in the pus from the foot; a stock vaccine was used, and after two inoculations the temperature came to normal.

A young colored woman, a nurse, acquired an infection of the foot. The wound was opened and drained. Cultures from the pus showed streptococci. The temperature before the operation was 104.8°. The usual wet dressings were applied, but the temperature continued high. Two days after operation the patient complained of the leg being painful and stiff. The next day the edges of the wound appeared discolored, and within a few hours signs of erysipelas appeared, and extended up the leg. These were painted with carbolic acid, followed by alcohol. The leg was greatly swollen and tender, and signs of phlebitis were present. The temperature was continuously high, between 103° and 105°. On the day erysipelas was noted a stock vaccine of streptococci was used, 50,000,000 being the initial dose. This was followed by no apparent result. The temperature and pulse remained persistently high for the next three days, when the second inoculation of 100,000,000 stock

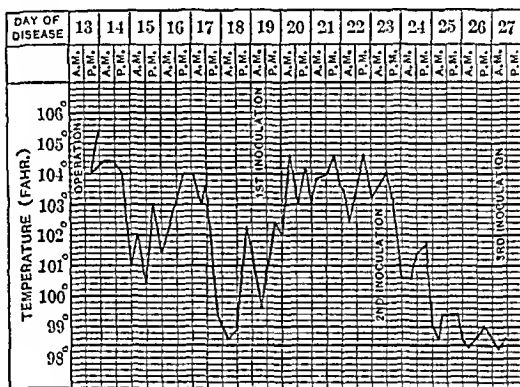


FIG. 8.—Temperature chart of Case VIII; infected foot; erysipelas. Stock vaccine used.

streptococci was given. This was followed by an immediate fall in temperature, the first in ten days, falling to 100.5°. The next day it did not go above 101.4°, and on the following day it came to normal and remained so (Fig. 8). The pulse likewise fell to normal coincident with the temperature, and the patient went on to complete recovery. It should be noted that surgical measures went hand in hand with vaccine treatment, particularly the treatment of the erysipelas with carbolic acid and alcohol painting, and also that the fall in temperature took place about the usual time in the course of erysipelas.

GENERAL SUMMARY. 1. Closely following Wright's method,<sup>1</sup> vaccines were made in eight cases from germs isolated from the blood, when this was possible; otherwise from pus taken from the point of local infection. Two types of vaccines were used—autogenous, and stock vaccine, made from germs secured from sources other than the patient. Of the cases reported, six received autogenous

<sup>1</sup> Transactions of Harvey Society of New York, 1907.

vaccine only; one received, first, stock, then autogenous vaccine; and one received stock vaccine only.

2. The cases reported comprise two of septicemia, one of malignant endocarditis, two of pyemia following appendicular operations, one of puerperal fever, and two of local infection.

3. Classified as to infecting organisms, there were five cases of streptococcic infection, one case of *Bacillus coli communis* infection, one case of *Bacillus mucosus capsulatus* infection, and one case of *Staphylococcus pyogenes aureus* infection.

4. In cases reported, improvement showed itself by a fall in temperature, reduction of pulse rate, and improvement in the general condition. The time taken to bring about these results varied from twenty-four hours to two weeks.

5. The number of inoculations given before the temperature came to normal permanently varied with the individual case, from three to seventy-five days, and from two to fifteen inoculations.

6. The number of organisms inoculated as a "dose" varied with the organism given. The following table shows the initial and maximum doses employed:

	Initial.	Maximum.
Streptococcus (3 cases) . . . .	50,000,000	100,000,000
Streptococcus (1 case) . . . .	50,000,000	200,000,000
Streptococcus (1 case) . . . .	2,500,000 (daily)	
<i>Bacillus coli communis</i> . . . .	25,000,000	200,000,000
<i>Bacilli mucosus capsulatus</i> . . . .	40,000,000	110,000,000
<i>Staphylococcus pyogenes aureus</i> . .	200,000,000	725,000,000

In streptococcic infections two methods of dosage were employed, large doses (50,000,000 to 100,000,000) twice a week; or small doses (2,500,000 streptococci) given daily. The latter method gave excellent results in two cases. As a rule, the doses are increased gradually, that is, by one-tenth of the initial dose.

CONCLUSIONS. 1. Bacterial vaccines, if properly used, can do the patient no harm.

2. Autogenous vaccines should be used when possible. Stock vaccines are uncertain, but they may be used when there is delay in securing autogenous vaccines.

3. The technique of preparing vaccines is simple and should be made a part of the routine laboratory work in every well-equipped hospital.

4. Chronic infections yield more readily to the use of vaccines than acute fulminating infections; and local processes are more easily controlled than general infection.

5. If a vaccine is to be of service, it will usually show results within one week or ten days.

Acknowledgment is made of valuable suggestions from articles by W. Gilman Thompson, M.D.,<sup>2</sup> and Drs. Barr, Bell, and Douglas,<sup>3</sup>

<sup>2</sup> AMER. JOUR. MED. SCI., August, 1909.

<sup>3</sup> Lancet, 1907, i. 499.

on the vaccine treatment of septic endocarditis, and Drs. Sutcliffe and Bayly<sup>4</sup> on streptococcic septicemia. I wish to acknowledge also the many useful suggestions of Dr. Thomas W. Hastings.

## THE PRESENT STATUS OF TUBERCULIN THERAPY.

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WHEN Koch, in 1890, introduced tuberculin as the long-sought cure for a dreaded disease, he was hailed as a deliverer. But Koch either did not understand his own remedy, or the scientific world misinterpreted his teachings. It is needless to dwell upon the disastrous results following the use of the original "Tuberculin," founded upon the principles of active immunity. It was not understood—large doses were given—and results were in many cases negative—in others fatal. But a few great and far-seeing minds realized that Koch had introduced a remedy which was destined to live. The majority of physicians dropped the new remedy with as much avidity as they had taken it up. Thanks, however, to a few German physicians, led by Koch, and to Trudeau, in this country, work upon tuberculin continued, developed, and improved until a new tuberculin is given us, and a new and better method of administration, with better results and no fatalities. Again the scientific world is inflamed and the pendulum is swinging the other way. Apathy has given way to enthusiasm, and it is well to pause a bit, lest this very enthusiasm lead us to discredit a method which, when used rationally and understandingly, is unquestionably a most valuable aid in the treatment of tuberculosis.

Before a physician is qualified to use tuberculin he should be able to answer satisfactorily four questions: (1) What is tuberculin? (2) What is the theory of its action? (3) What are the various kinds of tuberculin? (4) What is the dosage?

Let me briefly consider the first two questions together, from the theoretical point of view. Arloing and Courmont were the first to discover agglutinins for the tubercle bacillus. Their experiments showing that tubercle bacilli have agglutinating action and that antibodies were present in the blood of a tuberculous patient, were fought by the German observers, denied by Koch and his pupils, in particular Rabinowitz. Jürgens<sup>1</sup> is of the view that the agglutinins are only an evidence of the presence of soluble tubercle bacillus substances in the circulation. A few years after Arloing

<sup>4</sup> *Lancet*, 1907, ii, 367.

<sup>1</sup> M. Wolff and H. Mühsam, *Deut. med. Woch.*, 1908, No. 35.

and Courmont<sup>2</sup> came Bordet and Gengou, who presented the complement fixation theory in relation to the tubercle bacillus. Two years ago Wasserman and Bruck, working along the lines of these investigators, demonstrated antibodies in tuberculous tissue, and in the serum of persons treated with tuberculin. They named their antibodies "antituberculin" and thereby conceived a new theory upon which to base the action of tuberculin in the tissues and in the circulation. S. Cohn<sup>3</sup> carried out a series of interesting experiments in attempting to prove or disprove the theory advocated by Wasserman. He examined the blood of 77 patients, and in 10, clinically demonstrated as non-tuberculous, found no antibodies. In 14 "closed" cases of tuberculosis in the first stage he was also unsuccessful in his search. In 53 "open" cases of the second and third stage, 15 had antituberculin in the blood serum. These last named had not been treated with tuberculin, but had developed these antibodies spontaneously. Cohn therefore concludes that antituberculin is not an antitoxin in the true sense, and that the real nature of the Bordet and Gengou antibodies is undetermined—we only know that when tuberculin is introduced into the body it forms a complement (that constituent of the blood which Ehrlich, in his side-chain theory, says eventually destroys the bacteria) with the antibodies. Lüdke<sup>4</sup> demonstrated antituberculin in the blood serum of 17 out of 31 cases treated with tuberculin. Wasserman<sup>5</sup> tries to account for what is known as a tuberculin reaction by the presence of antituberculin in the tissues and for the cessation of a tuberculin reaction by the presence of antituberculin in the blood. Paul Ringer<sup>6</sup> puts this theory in plain English as follows: "The use of tuberculin is based upon the principle of artificial immunity, and any poison in the body has the power of stimulating the system to the production of antibodies." This, in a few words, represents what is considered at the present day the working theories for the action of tuberculin in the tissues and in the blood, namely, the agglutinin theory of Arloing and Courmont, the Bordet and Gengou antibody theory, and the elaboration of the second named, the antituberculin hypothesis of Wasserman and Bruck. It would be useless in the limits of this paper to go too deeply into them. They are extremely interesting, but are at best hypothetical and will no doubt in time be superceded by better and more practical theories. Let me group all theories of this nature together and agree with Tiegerstedt<sup>7</sup> who says that "all changes of immunity are protective adaptations of the body against harmful influences."

In the use of tuberculin our desire is to obtain an overproduction

<sup>2</sup> M. Christian and S. Rosenblatt, *Antibodies and Immunity in Tuberculosis*, Münch. med. Woch., lv, No. 39

<sup>3</sup> Berl. klin. Woch., xlv, 28.

<sup>5</sup> Deut. med. Woch., 1906, No. 12.

<sup>7</sup> Text-book on Physiology.

<sup>4</sup> Münch. med. Woch., 1908, Nos. 16, 15.

<sup>6</sup> Jour. Amer. Med. Assoc., 1907, I, 28.

of antibodies, call them by whatever technical name one may. We wish to build a defensive armament against which the tubercle bacillus and its ravages will be impotent. An organism can be immunized by injecting more poison into it with increased production of antibodies, that is, active immunization, or we can form antibodies by injecting into the infected individual the blood serum of a previously immunized animal, that is, passive immunization. In tuberculin therapy we aim to produce an active immunization. This immunity to tuberculin is a complete or almost complete tolerance to large doses of tuberculin, the latter dependent upon the judgment of the physician administering the dose, many of our best authorities being satisfied with obtaining even a relative immunity, that is, a tolerance to smaller doses. Hamburger<sup>8</sup> states that artificially acquired immunity to large doses of tuberculin is in many cases merely the result of the inability of the organism to react, due to a complete saturation with antibodies. He describes a test in substantiation of this assertion: A child of twelve months of age was supposed to be immunized but the autopsy showed the contrary. The individual who apparently was immune in reality did not respond to the tuberculin merely through inability to respond to a stimulus. Many physicians in undertaking a course of tuberculin therapy often forget this point. After giving repeated injections and getting no rise of temperature or untoward symptoms, they believe they are getting a state of immunization, when suddenly the patient dies and they find it difficult to account for the failure of the method. Therefore, one will see that this point of inability of the organism to react is of the utmost importance. On the other hand, what is of equal significance is the condition commonly known as a reaction.

Recent scientific investigations by Rosenau and Anderson,<sup>9</sup> Vaughn and Wheeler, and Wasserman and his pupils have done much to clear our ideas upon this question and thus guide us to a more rational and practical administration of tuberculin. Their work upon anaphylaxis or hypersusceptibility has demonstrated that in a tuberculous individual the cells have been already rendered hypersensitive by the action of the tubercle bacillus, and that when the tuberculin has been injected there takes place a division into two groups—poison and non-poison. The sensitized cells bind the poisoned groups and the well-known tuberculin action occurs. In the non-tuberculous individual the condition of anaphylaxis does not exist, and consequently the poison is freed slowly and discharged rapidly without causing any toxic symptoms which are the cause of a tuberculin reaction. The theory of anaphylaxis maintains that when foreign proteins, such as bacterial bodies, are introduced into

<sup>8</sup> Münch. med. Woch., iv, No. 42.

<sup>9</sup> L. S. Mace, California State Jour. Med., vi, No. 9.

the body, certain definite changes occur in the cell by which they are able to break up rapidly a succeeding dose of the same protein. If we accept this theory, then the reason becomes apparent why we should begin tuberculin therapy with minute doses of tuberculin and work up very gradually to the production of a complete, nearly complete, or relative immunity.

Before considering dosage let me review the composition of some of the various kinds of tuberculin on the market, and determine what our choice should be when beginning treatment of a tuberculous case. There are sold to-day between sixty and seventy varieties of tuberculin. Of these, I shall consider the following, the others being either modifications of these or having proved inefficacious:

1. Original tuberculin Koch (O. T.) is a pure culture of tubercle bacilli grown for several weeks in a 5 per cent. glycerin bouillon. This form of tuberculin contains all the soluble secretion products of the tubercle bacillus in a 50 per cent. glycerin solution.

2. New tuberculin (T. R.), introduced by Koch in 1897 to take the place of old tuberculin, the letters standing for tuberculin residue (Ruckstand). Koch having shown that tuberculin was a remedy, but that the great objection to it was its violent reaction, bent all of his energies to the preparation of a substance which should possess immunizing and curative powers, but which would not set up an intense general reaction in tuberculous subjects inoculated with them. Such substances he assumed must be sought in the material of which the tubercle bacillus was composed. After many experiments Koch succeeded in breaking up the bacilli and converting them into a form capable of absorption. For this purpose they were dried and rubbed in an agate mortar in such a manner that no entire particle of tubercle bacillus was left. He extracted all the soluble matter from the tubercle bacilli with distilled water, the resulting solution being T. O. (Tuberculin Obere). The insoluble residue which is separated from T. O., after being converted into a series of solutions, are in turn treated with 50 per cent. glycerin. Substances with only a small toxic effect upon tuberculous individuals are thus precipitated. These residual solutions are the T. R. and contain the whole of the immunizing substances of the tubercle bacillus in a form perfectly capable of absorption. 1 c.c. T. R. is made to contain 0.002 of dried residue. 100 c.c. T. R. is always obtained from 1 gram of dried tubercle bacilli. 1 c.c. of T. R. corresponds to 10 mg. of dried bacilli, but 100 c.c. of T. R. in reality contains only 0.2 gram of dried constituent. 1 c.c., therefore, contains only 0.002 of dry constituent. Ruppel<sup>10</sup> has cleared up a rather erroneous view which had been held for years concerning the amount of dried constituent in 1 c.c. of T. R. It was originally stated that each cubic centimeter contained 10 mg. of solid sub-

<sup>10</sup> Lancet, March 28, 1908.

stance. In reality, each cubic centimeter, as I have shown above, contains but 2 mg. The mistake arose from the fact that 10 mg. of dried bacilli is used to produce 2 mg. of active substance.

3. Bacillen Emulsion (B. E.) is made by using a finely pulverized virulent culture of tubercle bacilli, to one part of which is added 100 parts of distilled water and 100 parts of glycerin. The resulting emulsion contains 5 mg. of dried substance in each cubic centimeter of solution.

4. T. O. (Tuberculin Obere), the solution already described in the preparation of T. R. It is extensively used by some German physicians, but not very much in the United States.

5. Deny's Bouillon Filtre (B. F.) is a filtrate from bouillon cultures from the tubercle bacilli containing all the soluble products in the bacteria. Heat is not used in its preparation.

6. Bovine tuberculin is prepared in the same manner as other tuberculin, except that bovine tubercle bacilli are employed in its preparation.

I have thus far attempted to detail the theory of tuberculin, its action and its reaction, and the principal forms in use at the present time. Some physicians still cling to Koch's original tuberculin (O. T.) but in most countries and by the majority of observers it has been discarded for therapeutic use. Koch's New Tuberculin (T. R.) and (B. E.) and the (B. F.) of Denys are the three forms most in use to-day, with bovine tuberculin rapidly gaining popularity. In beginning the treatment of a case of tuberculosis, what should the choice of tuberculin be? I should say any one of the forms mentioned, so long as one is consistent in his dosage and careful in his observation. Most authorities today agree that unheated products act better than heated ones. The unheated products are (T. R.), (B. E.), and (B. F.) and one of these should be our choice. O. T. (original tuberculin) is a heated product. In my own work in the past two years I have used (T. R.) and (T. E.), principally the former, with such good results that I have no intention of discarding it altogether for the (B. E.), as so many are doing.

Among the tuberculins which are well known but not very popular might be mentioned Van Ruck's Watery Extract, Maragliano's Serum, Beranek's Tuberculin and von Behring's Tulase. At the recent International Congress at Washington, Oshijami,<sup>11</sup> of Japan, introduced a new serum called Tuberculo-Toxodin, a chemical preparation from tubercle bacilli applicable to incipient and feverless cases. He claims that his preparation dissolves the tubercle bacilli and transforms the toxic property, thus getting rid of any reaction. Very excellent results are claimed by this observer. Maragliano's serum is considerably used in Italy. Recently Monti,<sup>12</sup>

<sup>11</sup> Jour. Amer. Med. Assoc., xli, Nos. 21, 19, 17, 16, 15.

<sup>12</sup> Gazzetta degli ospedali, xxix, No. 2.



of Milan, has reported twenty-five cases of tuberculosis in children treated with it, with especially marked beneficial results in the surgical forms of tuberculosis, the benefit being less marked in the pulmonary forms. On the other hand, the Phipps Institute has experimented with this serum and claims it to be valueless.

The use of the bovine tuberculin is not yet thoroughly understood. In 1901 Koch, at the Congress of Tuberculosis in London, proclaimed the dissimilarity of human and bovine tuberculosis. His view was then challenged and has since been challenged, but he reiterated the same opinion as emphatically as before at the 1908 Congress in Washington. Men like Woodhead, Cohnheim, Aufrecht, Peterson, Ravènel, Arloing and Courmont, Theobald Smith, and Fibiger<sup>13</sup> all challenged Koch at a conference held in camera at this Congress, but the great master would not yield in his view or change his 1901 statement.

Pochin<sup>14</sup> recently reports some observations by which he tried to ascertain whether the action of the opsonins in bovine blood was the same with regard to tubercle bacilli of both human and bovine strain, or whether there was any marked differences which would indicate a distinction between the bacilli with regard to their susceptibility to the action of opsonins and therefore a difference in the resistance of the animal to infection by the bacilli of the different strains. He found marked differences. Without giving his experiments in detail, I quote him as coming to the conclusion that Koch is wrong in the emphatic views he promulgates as to the difference between the human and bovine tuberculosis. A. Cuff<sup>15</sup> reports a case of involvement of the apices of both lungs with cavity formation arrested by injections of bovine tuberculin, giving weekly injections for nine to ten weeks. N. Raw<sup>16</sup> claims that tubercle bacilli of human type produce phthisis pulmonalis, ulcerations of the intestines, and tuberculous laryngitis, and that tubercle bacilli of the bovine type produce tuberculous peritonitis, lymphatic gland tuberculosis, and tuberculous joints. He also believes that the acute miliary form is of bovine origin. Raw believes in giving bovine tuberculin in cases of pulmonary tuberculosis and Koch's T. R. in the surgical forms. He treated eighteen patients having pulmonary lesions with bovine tuberculin, getting very successful results, and 104 cases of surgical tuberculosis with Koch's T. R., with similar effect. He puts forth the hypothesis that the human body is attacked with two varieties of tubercle bacilli which may be present at the same time and which, generally speaking, are antagonistic to each other.

We see, therefore, in studying a subject like tuberculin and in reviewing the literature, how varied and conflicting are the views

<sup>13</sup> Jour. Amer. Med. Assoc., xli, Nos. 21, 19, 17, 16, 15.

<sup>14</sup> Lancet, September 5, 1908.

<sup>15</sup> Brit. Med. Jour., February 15, 1908.

<sup>16</sup> Lancet, February 15, 1908.

of careful observers with large amounts of material at their disposal, and we are unfortunately left very much to our own judgment in the choice of a proper tuberculin. There is as yet no unanimity of opinion.

We come now to the most important chapter of all in the treatment with tuberculin, namely, the dosage, and upon this point the scientific world is rather more in unison. We know that former bad results were mostly due to excessive doses of a serum not understood. I wish to warn against one very common error. Many physicians speak of a dosage of tuberculin in terms of milligrams. We should always stipulate the kind of tuberculin as it is put upon the market, since the amount of essential solid substance in the various forms differ. The beginning dose of tuberculin should always be very small. I believe we owe it principally to Wright that we are today giving proper and efficacious doses of tuberculin. His classical and now well-known work upon opsonins and the opsonic index, which in reality is a determination of the immunizing response of the blood, gave us an exact method of measuring dosage in the administration of tuberculin and gave us a better insight into what constituted a tuberculin reaction and how to avoid it. Although the administration of tuberculin by means of the opsonic index is being rapidly dropped by most observers, owing to the tediousness of its technique and the length of time consumed by the method, still the principle of small and carefully regulated dosage has been taught, and has practically revolutionized tuberculin therapy.

In my own work I have adopted with some slight modifications the dosage recommended by Trudeau.<sup>17</sup> I use T. R., German preparation, and have it put up in dilutions of from 1 to 20,000 to 1 to 10. I begin with 0.2 c.c. of 1 to 20,000 dilution or 0.1 c.c. of 1 to 10,000 dilution the former advocated for convenience, since it is more easily administered in the usual hypodermic syringe. My beginning dose then is 1 to 50,000 mg. of essential solid substance. (Trudeau begins with a dose of  $\frac{1}{100000}$  mg.) The initial dose is increased by 0.1 c.c. at intervals of two to three days and sometimes longer, until I am giving 1 c.c. of 1 to 100 dilution. I then increase my interval to a week and begin with 0.1 c.c. of 1 to 10 dilution, and when several doses of this dilution have been given I even extend the interval to two weeks. When I reach the dose of 1 c.c. of 1 to 10 dilution which is 0.1 c.c. of the pure T. R., or  $\frac{1}{2}$  mg. solid substance, I keep the patient upon this dose for some weeks. I seldom go beyond this dose, and find it unnecessary to give the patient large doses of the pure tuberculin.

This method has operated efficaciously in my hands in a number of cases, the detailed report of which I shall reserve for a future time when my series of cases shall have reached a sufficiently large number to make comparative deductions.

<sup>17</sup> AMER. JOUR. MED. SCI., 1906, cxxxii, 175.

It must be especially understood that a course of tuberculin therapy cannot be hurried. The patient must be told that it will require from six months to one year to accomplish, and the physician must realize the importance of increasing his dose very slowly. Reactions which were originally thought to be a necessary concomitant of tuberculin injections should be avoided. Trudeau has published some very extensive reports upon this subject in the last three years, and he claims that a reaction means that we have exceeded the patient's capacity for responding, and that it can and should be avoided. Denys lays down certain precautions: (1) Do not begin with too large amounts. (2) Do not raise the dose too rapidly or at too short intervals. (3) Do not again inject before all effects of a reaction have passed. (4) After a reaction, begin with a smaller dose than the one which caused the reaction. (5) Do not neglect to consider the patient's symptoms—such as headache, malaise, etc. I cannot improve upon these admonitions promulgated by Denys and adopted by Trudeau, rules which should be memorized and used as a guide by every physician attempting a course of tuberculin therapy. If they are followed, tuberculin can accomplish no harm, even though it may not produce an arrest of the disease.

To carry to a successful issue a course of tuberculin therapy requires careful observation and good judgment. The patient should always rest after an injection, and should never during the treatment overexercise or overstrain. Overexercise is often responsible for a reaction due to auto-inoculation. In fever cases especially the patient should be kept absolutely in bed until the temperature is normal, and then the tuberculin injections should be begun as previously indicated. Latham and Inman<sup>18</sup> advise absolute rest in bed as the only safeguard against auto-inoculation, and stipulate that the dose of tuberculin given must bear a definite relation to the amount of auto-inoculation, either occurring spontaneously, as in the fever cases at rest, or artificially induced, as in the afebrile cases up and about. Therefore, we cannot be too cautious in the conduct of our cases, having always before us the possibility of inoculation from the toxins circulating in the blood. We cannot be too cautious in beginning tuberculin injections nor in taking cognizance of all signs which occur during the treatment, and we must be especially careful to give the patient at all times sufficient rest.

Being sure that our beginning dose is small enough and that we are progressing with proper increase and at proper intervals, avoiding reaction, guarding against auto-inoculation, and never continuing the injections if perchance a reaction has occurred, the question then naturally arises, When should we cease injecting tuberculin? This again depends upon the judgment of the physician administering

the treatment. Some desire to obtain as far as possible an absolute immunization; others are satisfied with procuring a tuberculin tolerance. Personally, I aim only to effect the latter state. When all symptoms have passed; when only slight coughing remains; when the patient ceases expectorating; when the weight has been fully or almost fully restored; when the patient is able again to resume light duties without in any way feeling the effort of exertion, I stop tuberculin therapy, even though a few physical signs of tuberculosis may still be present in the lungs. In other words, when the disease from clinical appearance and signs may be confidently diagnosed as arrested, tuberculin injection should cease or, at most, be given at very long intervals.

I can best illustrate this by a case referred to me by Doctor Ethan Smith: This patient, aged twenty-three years, was kept on tuberculin for seven months; his condition at the beginning was most alarming; he had cough, high temperature, hemoptyses, numerous tubercle bacilli in the sputum, and he was considerably emaciated. He was kept in bed for three months, tuberculin therapy being given during this time, but not until the cessation of the hemoptyses and temperature. At no time after tuberculin injections were begun did he have any fever or any signs of a reaction. He steadily gained strength and weight until he was even heavier than before he took ill. He received his last injection of 1 c.c. of a 1 to 10 dilution of T. R. on March 6; at that time he weighed 141 pounds and was doing outdoor work. He still had a few tubercle bacilli in the sputum. I saw him again on March 21, when he was feeling well, had gained another pound, and had practically lost all physical signs. Upon this examination I could not detect any tubercle bacilli in the sputum. This patient has undoubtedly acquired a tuberculin tolerance, and the rest of his condition depends from now on upon the proper observance of hygienic laws.

The management of a case during injection is important. I have already referred to absolute rest in bed, preferably in the open air, for a long period of time, if fever is present or if the tuberculous focus is rapidly progressing. During this period the nurse or attendant, under the doctor's supervision, should keep careful records, especially of the temperature and weight. If the patient is ambulant, he should be taught to take his own temperature and to keep a record of the time and the amount of food he eats, his bowel movements, and any symptoms he may have. To treat tuberculosis properly, either with tuberculin or without it, requires a perfect understanding between patient and physician and a rational coöperation. The doctor must guide and instruct—the patient must be adaptable and observant. When my patients are ambulant, I especially instruct them about exertion. If possible, they must give up any active employment, although this is not always insisted upon. They are instructed to lie down from two to three hours after the injection.

Exercise is allowed in small doses at first and gradually increased. The beginning of a course of specific therapy often tries the patience of both physician and patient. At first no improvement is noticed; sometimes even a setback occurs. We must remember that this is a slowly progressing treatment extending over months, and we must constantly keep this fact before the patient. Often only after three months does the patient gain a little weight and a little hope and give the physician a little encouragement. In cases complicated with tubercular laryngitis the first encouragement is observed in the larynx. I have such a case now under treatment referred to me by Dr. A. S. Adler. The patient has an extensive lesion in the upper lobe of the right lung and a tuberculous laryngitis. The only improvement to date after six weeks of treatment is in the larynx. Dr. Robert Cohn, who is observing the larynx at intervals of two weeks, reports a very distinct change for the better.

Upon what class of cases should tuberculin be used? Here again opinions seem to vary. Lawrason Brown<sup>19</sup> in a recent article states: "The theory of the action of tuberculin plays an important role in the selection of patients. If it requires an active response on the part of the organism to produce a beneficial effect, it is useless to give it to patients who have lost all power of resistance and who fail to respond to stimulation." Therefore, it becomes apparent that the cases most desirable for tuberculin treatment are the incipient. Fever cases are undesirable, although Denys does not agree to this. Rapidly progressing cases should also never be given tuberculin. It may, however, be used with some degree of success in second and third stages. Pottenger's<sup>20</sup> statistics show that 65 to 90 per cent. of first stage cases get well, 30 to 65 per cent. of second stage cases, and only 5 to 10 per cent. of those in the third stage. Schrader, in his statistics, excludes only fever cases, and claims favorable results. Ritter<sup>21</sup> used tuberculin in 554 cases in his sanatorium, and comes to the conclusion that it has a favorable effect upon the disease. M. John states that in 200 cases treated with tuberculin the results are conflicting, proving negative in some of the apparently promising cases, while they were surprisingly good in others, even in some advanced cases.

During the last year reports have come of the use of tuberculin in surgical and genito-urinary tuberculosis, with favorable results. Edward Ochsner,<sup>22</sup> at the Washington Congress, reported that his cases of hip-joint disease were much influenced by the use of tuberculin and the final result hastened by it. P. Glässner<sup>23</sup> reports successful results in treating joint and bone tuberculosis with Marmorek's serum, and M. Strauss used Marmorek's serum in

<sup>19</sup> Boston Med. and Surg. Jour., 1908, clix, No. 4.

<sup>20</sup> Lancet Clinic, 1908, No. 7.

<sup>21</sup> Deut. med. Woch., xxxiv, No. 29.

<sup>22</sup> Jour. Amer. Med. Assoc., xli, Nos. 21, 19, 17, 16, 15.

<sup>23</sup> Deut. med. Woch., 1908, No. 29.

37 cases of various tuberculous processes in the bones, glands and bladder with gratifying results. N. Elsaesser<sup>24</sup> uses in surgical tuberculosis a combination of T. R. with Marmorek's serum. J. W. Walker<sup>25</sup> uses T. R. in tuberculosis of the genito-urinary organs. As already mentioned above, N. Raw uses Koch's T. R. with great success in all cases of surgical or bone tuberculosis. C. Kraemer<sup>26</sup> recommends tuberculin in the postoperative treatment of surgical tuberculosis, since he argues that the operation may cure the apparent lesion, but that the primary focus may still remain. This latter point has been proved in many cases by a positive tuberculin reaction, even after a total excision or extirpation of tuberculous glands.

Let us now pause and in conclusion consider carefully what constitutes the present-day status or conception of tuberculin as applied in the specific treatment of pulmonary tuberculosis and during the last year in nearly all forms of the disease. Is it a specific? I am compelled to reply in the negative. In the final analysis we can only regard tuberculin as a valuable adjunct to the hygienic and dietetic therapy of the disease. J. H. Pryor,<sup>27</sup> of Buffalo, most tersely states that a tuberculous patient "must have 18 square meals of oxygen per minute accompanied by three square meals of food per day." Trudeau,<sup>28</sup> who has used tuberculin over a longer period of time in more cases and more conservatively than any other man in the United States, shows that 18 per cent. more of treated incipient cases are living than of untreated, while 25 per cent. more of advanced cases who received tuberculin are living than of those who did not. He also says: "Many years ago, in spite of general denunciation of tuberculin and long before I knew anything about the statistical evidence, I had formed the opinion that tuberculin when administered had within certain limits a favorable influence on the course of the disease, and that the results of sanitarium treatment could be improved and made more permanent in many cases by its application. As years have passed I have seen no reason to change this opinion." Thus speaks one of our greatest authorities on this subject. We, with small experience compared with his, can only follow his lead. Tuberculin unquestionably is a valuable remedy in its present form and with the present improved method of administration, and is it not reasonable to hope that as the discarded tuberculin of 1890 was changed through the years into the valuable remedy of today, so may this remedial adjunct of today become a true specific in the future?

<sup>24</sup> Deut. med. Woch., 1908, No. 50.

<sup>25</sup> Practitioner, London, July 1908.

<sup>26</sup> Med. Klinik, iv, No. 4.

<sup>27</sup> Med. Record, January 4, 1908.

<sup>28</sup> M. Strauss, Marmorek's Serum in Surgical Tuberculosis.

**ADAMS-STOKES DISEASE WITH COMPLETE HEART BLOCK,  
SHOWING A CONSPICUOUS LESION IN THE PATH  
OF THE AURICULOVENTRICULAR BUNDLE.**

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THE strong bearing of Adams-Stokes disease upon the myogenic doctrine that has been so fruitful in advancing precise knowledge of heart disease, is a good enough reason for recording the most typical and classical case that I have ever encountered in experience or literature.



FIG. 1.—Adams-Stokes disease, showing the patient just recovering from a syncopal attack, with rapid pulsation visible in the depression above the clavicle.

The patient, Thomas M., a watchman, aged seventy-five years, was admitted to the Lincoln Hospital, on October 13, 1908, and died October 22, 1908. His family history was negative. He had previously had no important illness, except measles, whooping cough, and smallpox when a child. Later, he had muscular rheumatism, and twenty-five years ago had a sun-stroke, but had always

been considered a healthy, strong, hardworking Irishman. He drank whiskey moderately. Syphilitic history was denied.

On October 12, while in bed, he felt as though he was whirled around, and had a great buzzing in his ears, especially in his right one, in which he had been growing gradually deaf. After that he had three similar attacks, and came to the hospital complaining chiefly of these attacks and feeling weak. He said that the attacks and vertigo came on without premonition, and that between the attacks he felt perfectly well excepting that he was weak.

On admission, a physical examination, made by the house physician, Dr. Benjamin W. Seaman, and subsequently reviewed by me, showed a patient fairly well developed but poorly nourished, sitting up in bed with an alert and intelligent expression. He was able to answer questions perfectly, and gave a clear account of his symptoms. An examination of the chest showed the heart apex in the fifth space, three and a half inches from the median line. The heart was regular in action, except for occasional differences in the interval between beats, and there were no murmurs. Above the right clavicle venous

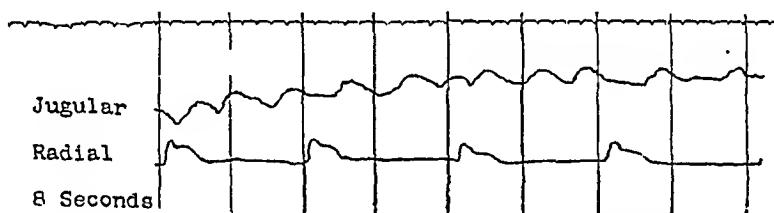


FIG. 2.—Tracing of the jugular and radial pulses during eight seconds.

pulsations were visible, two or three times more frequent than the apex beat. The patient's eyes reacted to light and accommodation. The tongue was protruded straight, and was deeply coated. The liver was not made out enlarged. The extremities were negative except that the knee-jerk was not obtained. No further physical signs of disease were obtained. The radial artery was not thickened, even to the degree that would be expected in a patient of this age.

The urine examinations revealed a specific gravity of 1020 to 1024, no albumin, no sugar; urea, 1.8 per cent. (9.1 grams in the twenty-four hours).

The diagnosis of Adams-Stokes disease was unhesitatingly made by all those who observed the patient. During his stay in the hospital, he was treated with potassium iodide, but his syncopal attacks recurred daily, and sometimes several times during the day. The iodide caused symptoms of iodism, and was discontinued. This patient was under observation for nine days, and at the end of that time he became delirious, and one morning his pulse dropped to 20, his respirations rose to 28, his temperature fell to 96°, and he died suddenly.



The pulse-respiration ratio, recorded while under observation, at intervals of four to eight hours, was as follows: 38 to 20, 40 to 22, 36 to 24, 36 to 24, 32 to 20, 30 to 22, 32 to 20, 34 to 24, 32 to 20, 36 to 22, 34 to 28, 30 to 20, 34 to 18, 30 to 20, 32 to 18, 34 to 28, 32 to 22, 30 to 20, 30 to 20, 28 to 20, 30 to 20, 30 to 20, 32 to 24, 32 to 24, 28 to 20, 34 to 24, 32 to 24, 36 to 24, 30 to 20, 32 to 24, 32 to 24, 28 to 29, 26 to 24, 30 to 24, 32 to 20, 28 to 24, 28 to 24, 28 to 24, 26 to 20, 30 to 24, 26 to 20, 28 to 26, 24 to 28, 20 to 28.

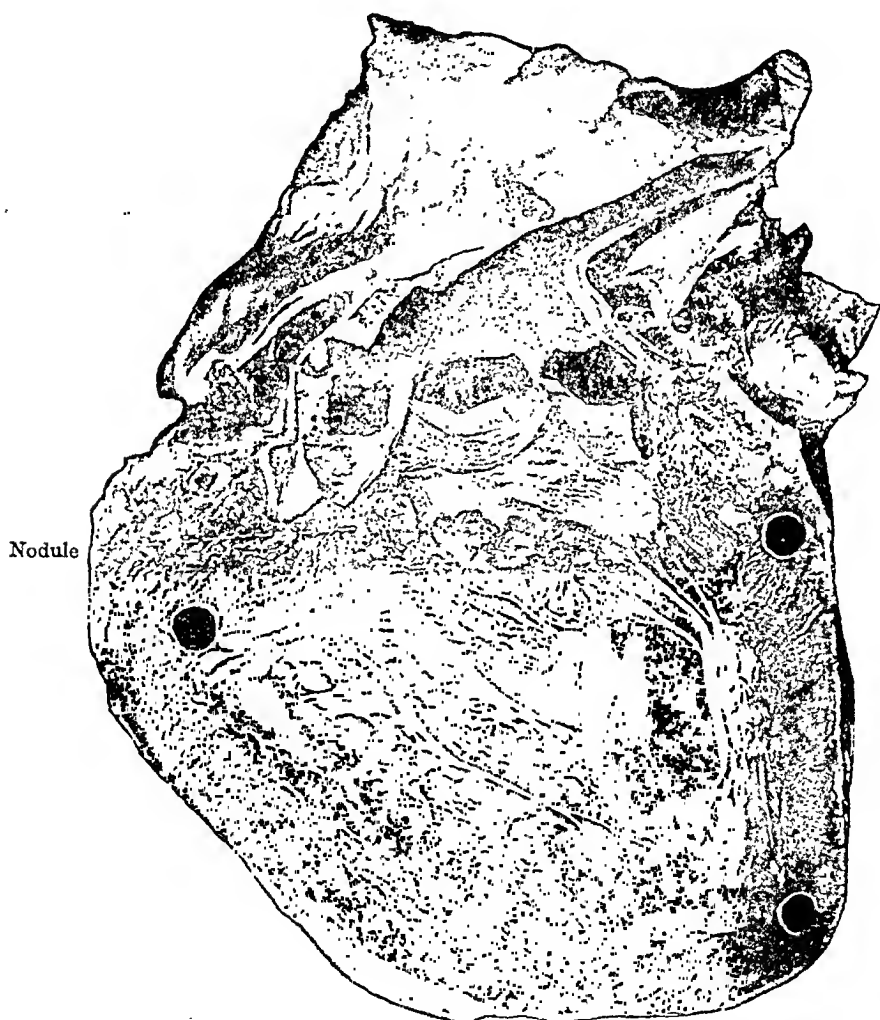


FIG. 3.—Heart showing a calcareous nodule in the region of the bundle of His.

The photograph of the patient (Fig. 1) shows him just recovering from a syncopal attack. In the depression visible above the clavicle the comparatively rapid jugular [pulsations could be seen. The

tracing (Fig. 2) shows the radial and jugular pulse during eight seconds.

The postmortem examination was made by Dr. J. H. Larkin. The heart (Fig. 3) showed a calcareous nodule, situated precisely in the path of the bundle of His. This nodule was evidently the cause of the complete heart block observed during life.

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## THE TECHNIQUE OF OPERATIONS ON THE LOWER PORTION OF THE URETER.<sup>1</sup>

BY CHARLES L. GIBSON, M.D.,

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IN performing any operation, but more particularly in the abdomen, a sufficient exposure of the operative field is necessary for efficient and safe work. There are few parts of the body where it is so difficult to obtain these conditions as in operations at the pelvic outlet, particularly when seeking to remove stones situated in that portion of the ureter which lies below the pelvic brim. Of course, it is easy enough to make a ruthless incision which resembles the technique of the morgue rather than the operating room; but in this country, certainly, we very justly do not consider that the mere completion of an operation spells success: we judge its value by the end results. For it cannot be said to be a gain for a patient to have the trouble caused by the presence of a ureteral stone replaced by a huge and weak scar which allows of eventration of the abdominal contents, a condition of permanent danger and discomfort.

In work which entails opening the ureter, I assume that the weight of evidence is in favor of procedures which do not permit urine to find its way into the peritoneum. Other debatable points are: Shall we attempt to close an intentionally opened ureter, and, shall we provide prophylactic drainage against a possible urinary leak—in other words, shall we deliberately relinquish the opportunity to secure complete closure and union of this abdominal wound?

In my judgment the ideal method of performing operations on the lower ureter should fulfil the following conditions: The incision of the abdominal wall should be of such a size and situation as to give an ample exposure for the easy recognition of the ureter, the necessary manipulations, and security from injury to the other pelvic structures, particularly the iliac vessels. The incision should be extraperitoneal. It should be possible to make

<sup>1</sup> Read at a meeting of the American Association of Genito-urinary Surgeons, June 1, 1909.

the ureter so freely accessible that any incision in it can be as easily and accurately repaired as a lesion of the intestine. There should be no unnecessary trauma or malhandling of the tissues, so that the completion of the operation should leave a perfectly dry field, doing away (when the continuity of the ureter has been restored) with the necessity of drainage—a prophylactic measure against subsequent hernia. The incision of the abdominal wall should be so planned as to produce the least damage, allowing when it is closed without drainage a firm union without risk of hernia. Finally, the whole operation should be so simple, so free from annoying hemorrhage or other pitfalls, that it can be performed without undue waste of time—half an hour or less.

These ideals, I believe, can be realized by a suitable exposure of the ureter and the lower pelvis by an incision which I offer for consideration.

The description of the incision and the various steps are as follows: The original idea of the incision was to utilize the advantages of the Stimson-Pfannenstiel incision, which is used frequently, particularly in gynecological laparotomies. I have used it in probably a hundred such laparotomies, and believe it is the least likely to be followed by hernia. Familiarity with the anatomy of the abdominal wall and abdominal incisions generally will be necessary for a successful execution of the several steps.

The skin incision runs from the mid-line about a finger's breadth above the pubes, horizontally outward nearly parallel to Poupart's ligament at first (Fig. 1), and curves rather sharply upward at its mid-point to end about opposite the anterior superior spine of the ilium. This incision is deepened in the same line through the aponeurosis of the external oblique and the internal oblique muscle,—the latter is the only structure which suffers any real damage, and only to a slight degree, for the lower part of the incision runs about parallel to its fibers, only the ascending leg cuts across a small part of these fibers. The incision stops short of the transversalis, which is not disturbed at all. With efficient retraction of the upper flap the external border of the rectus muscle is identified (Fig. 2) and the *fascia* of the transversalis is now divided by a vertical incision close to and parallel to the rectus—that is, at *right angles* to the original incision. Two retractors are now inserted, the outer one retracts the cut edge of the transversalis outward, the other (Fig. 3) pulls the rectus muscle well toward the mid-line. A generous space is thus obtained, situated well toward the mid-line (the lower part of the ureter is practically in the mid-line, and difficult of access by other extraperitoneal exposures). The floor of this space is occupied by the peritoneum. The patient being in a complete Trendelenburg position, the peritoneum is easily and gently pushed away, and a free access to the pelvis is secured. So ample is the space and view, that the whole hand can be introduced under the control of

suprapubic operation as compared with the perineal route; while the percentage of operative risk favors the selection of the perineal operation. Yet a progressive decrease in mortality is apparent in both instances, and up to now the perineal technique has probably received much greater attention than the high operation. I am disposed to believe that the future will develop the latter operation to a considerable extent.

As it is true, as is clearly set forth by Waston, that the suprapubic is a complete operation, having a large percentage of cures and a small percentage of operative complications, and is rapid of performance, under conditions which afford free access to the gland, it is a matter of serious importance that effort should be made to improve the technique and bring down the mortality rate.

This communication is devoted to the consideration of six cases of suprapubic prostatectomy, representative of different phases of the subject, operated upon in the last six months, except one of them, which was operated upon somewhat more than one year ago.

A brief resume of the cases is as follows: The patients are aged seventy, seventy-two, sixty, seventy-five and sixty years respectively. The duration of symptoms was from one to twenty years. Urination: Complete retention in three cases; frequent and difficult urination in the remainder, with residual urine from four to twelve ounces. Pain was present in a greater or lesser degree in all cases. Infection had occurred in all of them with one exception; that is to say, the urine was cloudy and bacterial, and in three there was ammoniacal decomposition. The urethral length varied from eight and one-half to nine and three-quarter inches. Rectal examination revealed the prostates to vary in size from that of a slight median enlargement to five times the normal dimensions. Bladder exploration was possible in all but one case; and it was possible to recognize with the sound an intravesical median projection. Examination of the urine showed moderate implication of the kidneys in half the cases. Other complications were a stone in one case, glycosuria in one case, carcinoma in one case, and one patient suffered from extreme obesity.

Operation was primary in all cases with one exception, in which it was performed secondarily to a previous perineal prostatectomy. The operation was done in two steps in one case, on account of the unsatisfactory general condition, very foul urine, and much prostatic congestion. Convalescence was prompt and uninterrupted in all except one case, in which it was protracted.

The latest report following operation varies from one to thirteen months. The result has been return of voluntary urination in all cases; and elongation of interval between the urination from complete retention and fifteen minutes to one hour frequency before, to a minimum of two hours and a maximum of six hours following operation. The urine has become clear in three cases, and remains

cloudy, but not decomposed in three. A swollen testicle occurred in three cases following the operation; in all of these cases there was a history of previous trouble in the testicle. In one case active epididymitis occurred before the operation; a double vasectomy was performed, and no relapse occurred after the prostatectomy. In the other cases there had been no previous trouble with the testicles, and none occurred after prostatectomy.

The operative technique followed is practically the same in all cases. Special attention is given to certain details to facilitate the operation, shorten its duration, and enable the hastening of post-operative convalescence. Of the last consideration, the most important is that of bladder drainage.

The patient is brought to the operating room with the bladder washed. The anesthetic used has been in most instances ethyl chloride and the drop ether method. The bladder is emptied, and while the catheter is left in place the patient is immediately put into the Trendelenburg position. An incision is made above the pubis, about three inches in length, separating the muscles and exposing the pre-vesical fat. An assistant now inflates the bladder with air, while the wound is separated by retractors. The structures overlying the bladder are stripped upward to the upper extremity of the wound with a piece of gauze. Incision is now made through the bladder, running well downward. This incision may be enlarged later, after the exploration with the finger has been completed.

Exploration with the finger is usually sufficient to give an adequate idea of the prostatic growth, but retractors may be inserted and ocular observation made if desired. In one of the cases of this series the cancerous nature of the prostatic growth was recognized by palpation at the time of operation. A place is selected for the incision of the mucosa over the prostatic growth, which is usually to one side of the median line at a point where the lateral and median growths meet. Into this incision the bare finger is inserted, and by gentle manipulation it is ascertained that a good line of cleavage is obtained. Separation of the prostatic growth is then accomplished with the aid of the gloved finger of the other hand in the rectum.

As to the all-important matter of drainage, I have for two years past been using a double tube, one large and one small, for continuous irrigation; this in the first twenty-four to forty-eight hours is an important feature, to prevent blood-clotting inside the bladder. When in Europe last year I found that in Paris the surgeons were using a similar double current tube, designed by Dr. Marion, which did not differ in principle from those that I had been using for some time previously. This resembles the Freyer tube in its unusually large size, with the addition of a small catheter-like tube for irrigation (Fig. 1). The extra large size is intended to permit free evacuation and prevent retention of clots. Freyer

uses an extraordinarily large tube without any irrigating attachment. I have found of late that drainage is just as good with the irrigating attachment when a smaller tube is used, allowing the insertion of two or three stitches to close up the bladder wound so that shortening of the convalescent period is the result.

The size of the tube used is from three-eighths to five-eighths of an inch in diameter, with the small catheter attached; besides this, however, I often use an indwelling catheter in the urethra, both because it is useful to irrigate through, should the other attachment become clogged, and because it smooths the newly forming posterior urethra during cicatrization, and is already in place for use after the bladder tube is removed, thus avoiding the unnecessary bruising of the tissues which sometimes occurs upon the first introduction of a catheter after operation.

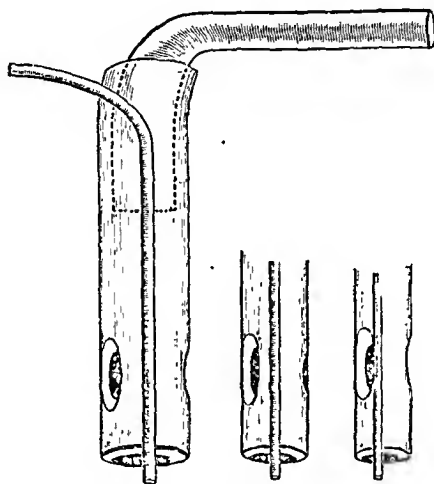


FIG. 1.—Suprapubic drainage tubes with irrigating attachments.

The prime object of good drainage is to keep the bladder clot-free and the patient comfortable during the first few days. I find that the method described adequately fulfils these conditions. It is at the period when the suprapubic tube becomes somewhat loose that we have experienced difficulty in keeping the urine from overflowing alongside. Various systems of siphonage have been resorted to, but have not proved successful. I have employed a system of siphonage designed many years ago, and have had constructed an apparatus on the same principle as that of Dr. L. W. Bremnerman, of Chicago, which is not continually getting out of order, and keeps the patient dry. This (Fig. 2) consists of an irrigator jar which empties at slow speed into a tip cup; this overflows at regulated intervals into a funnel, and thus provides intermittent siphonage of the bladder. This siphonage is especially useful during the first five to seven days after operation, when it is important to keep the suprapubic

wound clean and as dry as possible, so as to promote union of the parts sutured.

The period when it is most difficult to keep the patient dry and comfortable is that between the time when the suprapubic tube is taken out and before the suprapubic fistula is sufficiently healed to permit voluntary urination. During this period I utilize the

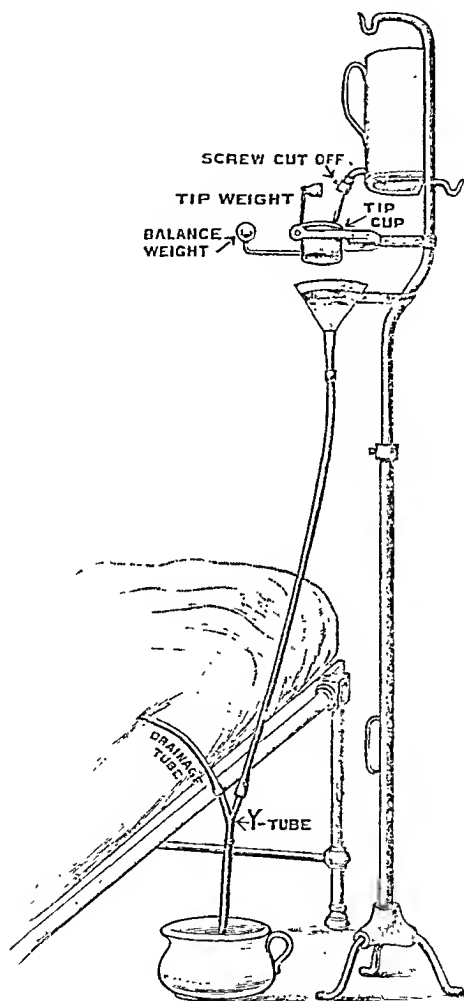


FIG. 2.—Apparatus for automatic siphonage of the bladder.

indwelling catheter in the urethra, strapping the suprapubic wound over tightly with adhesive straps. This stage is reached in a much shorter period when the drainage opening left at the time of operation is comparatively small, the tissues not lacerated, and early granulation encouraged by keeping the wound comparatively clean and dry by means of satisfactory drainage provision. The catheter is kept in place from four to five days to a week, and then voluntary urination occurs with moderate leakage.

In one of the cases of the series reported, a fistula remained for a number of months, but this was on account of deterioration in general health and the great obesity of the patient. Ultimately satisfactory closure occurred.

The cases, briefly, are as follows:

CASE I.—April 1, 1908. Aged seventy years; duration twenty years. There was complete retention. The prostate was very large, and much congested. The urine was excessively purulent and foul. Both rectal touch and bladder exploration recognized a good-sized median intravesical projection. The general condition was much depreciated, on account of extreme obesity, diabetes, and general toxemic debility.



FIG. 3.—Case I. Bilateral and median prostatic hypertrophy and vesical calculi.

The operation was done in two steps: a primary suprapubic drainage, at which time two calculi were removed; and ten days later complete prostatectomy (Fig. 3). At this time the patient's general condition showed marked improvement, and as a result the removal of an extensive growth caused the patient little or no surgical shock.



The postoperative convalescence was long, on account of slow healing of the wound, due to great obesity. A fistula persisted for several months, but eventually healed entirely. An intercurrent epididymitis occurred and suppurated.

At present the patient urinates every four to six hours, the bladder empties, the general health is excellent, and sugar has entirely disappeared from the urine.

*Remarks.* This case is an example of advanced prostatic hypertrophy producing complete retention; and a bad general condition due to toxemia, great obesity, and glycosuria. It illustrates the conservative effect upon both general and local conditions of a preliminary drainage as a preparatory measure.

CASE II.—November 29, 1908. Aged seventy-two years. This patient has been getting up at night to urinate once or more often for a year, and in the past six months the frequency has become much increased; at times urination has been as frequent as every quarter to one hour, and at night six times. No instrument was

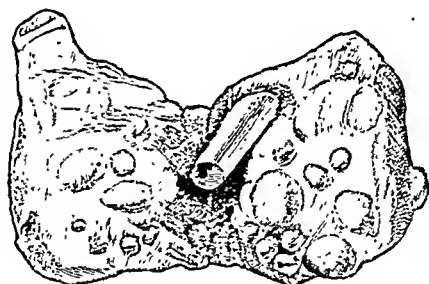


Fig. 4.—Case II. Symmetrical prostatic hypertrophy, showing carcinomatous foci.

passed until three weeks ago, when eight ounces of residuum was obtained. He never passed blood spontaneously. The urine was clear and sparkling. The prostate per rectum was as large as a golf ball, and of unusual hardness. The patient had lost six pounds in weight.

On December 1, 1908, suprapubic prostatectomy was performed. The prostate was enucleated with difficulty from a rather thickened capsule, a piece of which was also removed for laboratory examination (Fig. 4). The patient made a good recovery, left the hospital, and returned to his home in South Carolina, about three weeks after the operation. The laboratory reports showed carcinomatous foci throughout the gland; but the capsule proved to be simple inflammation, and contained no signs of neoplasm. The patient reports excellent health in December, 1909 (one year after operation); his condition has remained satisfactory so far as his own or his attendant doctor's observation is able to determine.

*Remarks.* The suprapubic operation in this case permitted thorough inspection of the vesical cavity and complete removal

of the gland, without disturbing the bladder function. Whether a more extensive operation would afford a greater immunity from recurrence is a question.

CASE III.—Aged sixty years. The patient's history dates back four years, when he commenced having frequency and urgency of urination, following an exposure and cold, when he had his first attack of complete retention. The frequency and urgency of urination gradually became worse until the demand was almost constant. Two years ago this condition reached its most acute stage, when the patient was able to urinate but a teaspoonful at a time, and compelled to sit down to accomplish this. At this time he entered one of the large city hospitals for relief, and a transcript of the history shows that he was operated upon in April, 1907. A description of the operation states that through a V-shaped incision the bulbo-urethra was reached; an opening was made into the median portion upon a staff, the capsule of the prostate exposed, and a prostatic retractor introduced through the opening in the membranous urethra; through incisions made in the capsules on both sides of the prostate, one-half inch from the median line, the prostate was removed in three pieces.

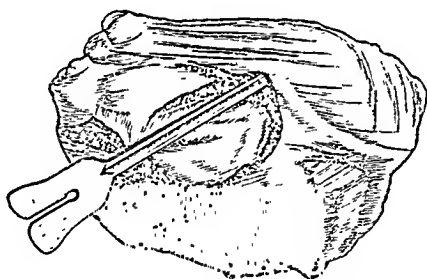


FIG. 5.—Case III. Large median lobe left by a previous perineal prostatectomy.

In April, 1909, he appeared at the Polyclinic Hospital with almost complete retention of urine, great difficulty of urination, and it was not possible to introduce a Nélaton or woven silk catheter. A metallic catheter was introduced with some difficulty. The finger introduced into the rectum felt, with the sound on the floor of the bladder, what seemed to be a prostatic growth of a size much beyond the normal. The urethral length was nine inches.

In the early part of March, 1909, the patient was subjected to suprapubic prostatectomy and a large symmetrical growth was removed, including the posterior section of the prostatic urethra (Fig. 5). The patient made a good recovery. The wound healed readily, and voluntary urination returned. A certain amount of dribbling, however, has persisted between the urinary acts.

*Remarks.* This case illustrates the ineffectual results of an attempt at complete removal of the prostate by a deliberate and, from the description, carefully performed perineal operation. On

account of a remaining middle lobe, of large size, producing complete retention, a secondary operation was necessary; the large intravesical projection was readily removed by a suprapubic operation, which was evidently not found accessible at the perineal operation.

CASE IV.—October 4, 1908. Aged sixty years. The patient complained of complete retention of a few days' duration, following upon more or less acute irritability of the bladder for several weeks back, when he thought he contracted an acute gonorrhea; before this there was nocturnal frequency. He had had gonorrhœa two years before, but no previous retention. The prostate per rectum was two and one-half inches in diameter, generally symmetrically enlarged.

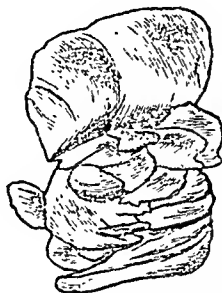


FIG. 6.—Case IV. General prostatic hypertrophy with a median projection.

The prostate (Fig. 6) was removed by enucleation in one piece through an incision in the vesical mucosa. The patient was up in the ward in two weeks, and made an excellent recovery without post-operative complications, the bladder emptying completely, and the urine coming clear.

*Remarks.* This was a borderline case, that might have been done as well by either perineal or suprapubic route. The result could hardly be improved upon.

CASE V.—February, 1909. Aged seventy-five years. Complete retention the day previous to admission. Symptoms of prostatitis of seven years' duration. There had been two previous attacks of retention, two and seven years ago. The prostate per rectum was four inches in diameter, and felt globular and firm; it extended upward centrally.

The urethral length was ten inches. Exploration with a sound detected a median obstruction.

Complete removal of prostate was effected suprapubically without difficulty (Fig. 7). Continuous drainage was provided in the usual way. Suprapubic drainage was used for ten days, following which a change was made to an indwelling catheter, which was retained for about two weeks; during this time the suprapubic sinus

healed, and voluntary urination and complete emptying of the bladder were satisfactorily accomplished.

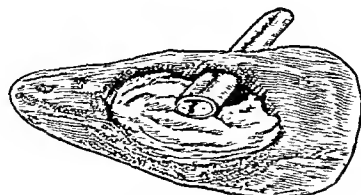


FIG. 7.—Case V. Middle lobe of the prostate causing complete occlusion of the urethral orifice.

CASE VI.—Aged sixty years. This patient's symptoms had existed for one and a half years, during which period he had had increasing difficulty in passing water, and greater urgency and nocturnal urination. On November 30, 1908, he had almost complete retention of urine, being able to pass but one or two ounces without the use of a catheter, and in the spring of 1909 he became practically entirely dependent upon the use of a catheter. The urine was cloudy, but not decomposed. The urethral length was nine and one-half inches. Rectal examination showed a symmetrically enlarged prostate, extending backward beyond reach. The bladder exploration revealed resistance upon the floor, as of a middle

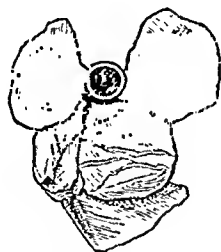


FIG. 8.—Case VI. A median lobe of the prostate with two bilateral projections.

lobe. The kidneys were not affected. The patient had constantly recurring swollen testicle, and on this account was primarily subjected to a double vasectomy, which afforded complete relief.

On April 30, 1909, suprapubic prostatectomy was done, the prostate being removed in three portions (Fig. 8). The middle lobe, which showed a symmetrical enlargement, imposed upon the urethral orifice and two other symmetrical bodies from the lateral region. The patient had no untoward symptoms. He was sitting up out of bed in a week. In about ten days the drainage tubes were removed and the indwelling catheter effectually drained the bladder, there being only slight moisture at the site of the suprapubic wound. At the end of the second week the catheter was removed and the

patient was able to urinate voluntarily, emptying the bladder, and the wound sinus was practically closed.

*Remarks.* Cases V and VI illustrate simple, straightforward suprapubic prostatectomies, presenting ideal results and the accomplishment of satisfactory drainage by means of irrigation and siphonage with a moderate sized tube; this permitted suture of the bladder walls around a small drainage opening, which, combined with the use of a retained catheter, was the means of affording a short and comfortable convalescence and early return to voluntary urination.

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## THE PRINCIPLES AND TECHNIQUE OF THE WASSERMAN AND NOGUCHI REACTIONS, AND THEIR COM- PARATIVE VALUE TO THE CLINICIAN.

By D. M. KAPLAN, M.D.,

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INTRODUCTION. A syphilitic taint in an individual is of importance not only to the diagnostician and therapist, but also to the social economist. A means for its detection becomes a valuable contribution to our diagnostic methods, the more so the greater the sensitiveness of the reaction as established by its coincidence with clinical findings. The Wasserman reaction, based upon an ingenious principle, worked out by Bordet and Gengou, gives to the experienced laboratory worker a very satisfactory means of diagnosing syphilitic affections, even in individuals who were infected years ago, of course excluding a dormant condition or patients at the end of a successful treatment. Having analyzed over 700 sera from dubious, negative, and distinctly luetic individuals, I venture to give my results with the Wasserman and Noguchi tests, considering as an introduction the various principles of immunity upon which the reaction of complement deviation depends.

REACTION OF THE ORGANISM TO INFECTION. When a child is affected with diphtheria, the poison produced by this bacterium produces most of the symptoms of the disease. When the patient survives, it is possible to demonstrate in his serum substances which are capable of neutralizing the toxin of the diphtheria bacillus. The antitoxin to this disease is extensively manufactured by drug concerns by infecting horses with diphtheria, and at a convenient time withdrawing from the jugular vein some serum which contains the antitoxin. We learn from this simple exposition that an organism infected with a certain disease, in order to protect itself, produces in its body a substance which neutralizes the bad effect of the invading factor. Not only does the animal body respond in such a specific manner against bacteria, but the same is evident when we

inject certain acellular vegetable poisons or cells from another animal.

It is by no means a difficult task to produce in the serum of a suitable animal substances which will destroy the red blood corpuscles from another animal. This is accomplished by injecting into the animal such cells as we wish to destroy. One may produce in the rabbit (the animal used for the production of antibody) substances which are capable of destroying sheep red cells, bovine red cells, or human red cells, the specific quality depending upon the cells used for immunization.

In order to be able to grasp the steps in the Wasserman reaction it is indispensable to be acquainted with the steps involved in demonstrating antibodies of any kind formed accidentally (by disease) or purposely (in immunizing) in the body fluids of an animal. Ehrlich showed long ago that in the demonstration of antibodies, or, as he called them, amboceptors, three distinctly different substances are required in order to form a complete reaction: first, the cell or poison against which we wish to immunize, or, more plainly, against which we desire to obtain an antibody; second, the antibody (or amboceptor) obtained by repeated injections of the special cell or poison into the rabbit (or any other suitable animal); third, a completing substance—the complement. This latter substance is present in variable quantities in the sera of all animals, its quantity being rather constant in guinea-pigs. It is destroyed by heating serum at  $56^{\circ}$  or  $57^{\circ}$  for one-half hour, and is similarly affected by various other physical agents. This is not the case with antibodies which are comparatively thermostable. We have, then, three factors: (1) A cell to be destroyed or a poison to be neutralized; (2) a substance capable of doing this—the amboceptor or antibody; and (3) a completing substance, without which the reaction cannot take place—the complement.

Ehrlich and others, in order to impress the reaction upon the minds of men interested in immune processes, made use of diagrams. To make it still more familiar, let a lock represent the cell, a key which fits it the antibody, and the hand that will turn the key the complement. By giving a lock to a smith we can get a key made to fit the specific lock exactly. When we inject cells we get an antibody which exactly fits the cell injected, and the same is true when we inject a bacillus or a poison. All these substances capable of producing antibodies (antibody generators) are known as antigens.

To determine whether a bacterium was killed or a poison neutralized by being exposed to the action of a specific amboceptor is not as simple a process as the demonstration of the destruction of red blood corpuscles by an amboceptor directed against them. A suspension of red blood corpuscles minus amboceptor and complement gives an opaque red mixture; when we add the amboceptor plus complement and incubate at  $37^{\circ}$ , the opacity disappears and a clear red

fluid results. It is apparent that hemolysis or destruction of red cells is a phenomenon that can readily be seen *in vitro*, and its presence signifies that the three substances spoken of above are present in the test-tube. If any one of the three is not there, or is present in an inactive state, the red cells will remain unaffected and the mixture will retain an opaque red color.

**HEMOLYSIS.** The phenomenon known as hemolysis depends upon the destruction of red blood corpuscles. There are many reagents capable of doing this, such as distilled water, acids, and alkalis. It is also possible to form in warm-blooded animals substances which will bring about hemolysis against certain red blood cells. This is accomplished by injecting an animal (a rabbit or goat) with the cells of a sheep or any other animal. The serum from such a rabbit, when brought in contact with the cells of the sheep, will cause the mixture to become clear (hemolysis). The same amount of serum from an untreated rabbit will have no effect on a similar suspension of sheep cells. The substance produced in the rabbit's serum is known as the antish sheep amboceptor, and together with sheep cells and complement (from a guinea-pig) is known as a hemolytic system.

**THE BORDET-GENGOU PHENOMENON.** The principle applied in the Wasserman reaction depends upon a test originally devised by Bordet and Gengou in 1901. At that time these authors conceived the idea of demonstrating *in vitro* the presence of unknown amboceptors (or antibodies) by attempting to fit on to them the corresponding antigen. It is clear that in order to do this, complement is absolutely necessary. Supposing, then, the antibody at hand to be from a patient who suffered from typhoid, this antibody ought to anchor itself to the organism responsible for its specific production, the typhoid bacillus, or suitable extracts made from typhoid cultures. This actually takes place and, if complement is present, forms an undisruptible triad; in other words, typhoid antigen is bound to the available complement by the typhoid amboceptor. If we should introduce into the very same test-tube a mixture consisting of sheep cells and some antish sheep amboceptor, no hemolysis will take place, for the simple reason that in order to do so complement is necessary, and, as said before, the available complement has been bound—or deviated—by the preëxisting well-fitting typhoid antigen and typhoid antibody. If the serum of the patient had not contained typhoid antibodies (in case of acute miliary tuberculosis), the complement would not have been bound to the typhoid antigen, but would have been left free, and a hemolytic system consisting of sheep cells and antish sheep amboceptor would be completely laked—or dissolved—for the available complement was left free to act, was not deviated or bound up.

We learn from the above exposition that in order to prove the presence or absence of certain antibodies, we make use of the

phenomenon of bound or unbound complement, utilizing a hemolytic system simply as an indicator. Exactly the same principle is applied to the serum diagnosis of syphilis. Unable to produce a growth of *Spirochaeta pallida* upon any culture medium, we have to be contented with organ extracts containing them in greatest numbers; for this purpose the liver of the luetic foetus furnishes the requirements. The extract produced is known as luetic antigen, and need not confuse anybody, for we know that an antigen is a body capable of forming antibodies. If an individual has had syphilis some years ago, he would also have syphilitic antibodies in his serum which, when brought in contact with the extract from the syphilitic liver, would invariably, as pointed out before, bind complement, and a hemolytic system (sheep cells or any other red cells with the corresponding amboceptors) will never be affected on account of lack of complement.

I hope the very rudimentary style of offering to the reader an explanation of the phenomenon of complement deviation will be remembered on account of the simplicity of terms used and the simple analogy with more familiar subjects. I will now consider the actual steps of the reaction, giving it in detail and as plainly as the untrained worker desires it.

**TECHNIQUE OF THE WASSERMAN REACTION.** *Principle Involved.* As mentioned before, antibodies will attract complement if the antigen responsible for their formation is present in the same test-tube. In the Wasserman reaction a serum containing antibodies capable of uniting with the antigen used (a substance containing lipoids), and thus deviate the introduced complement, will not permit hemolysis to occur if sheep cells and their antisheep amboceptor are subsequently placed in the same tube, and for obvious reasons—the complement was bound or deviated previously by conditions suitable for such an interaction. If the patient's serum does not contain the required antibody, the introduced complement will remain unbound and in a fit condition to destroy the sheep cells when subsequently introduced with their antisheep amboceptor.

*Modus Operandi.* (1) Obtaining blood from patient: A fairly stout piece of rubber tubing is placed a little above the elbow and held snugly in place by an artery clamp. Do not obliterate the pulse. This brings into prominence the veins at the bend of the elbow. To a stout hypodermic needle (I use a 19 bore—one and one-half inch needle) attach a two inch piece of rubber tubing. Holding the free end of the rubber tubing in an ordinary sterile test-tube, quickly plunge the needle into the most prominent vein; if expertly done, the patient will hardly feel it and the blood will immediately begin to flow. About 6 to 10 c.c. of blood is withdrawn and placed in the ice box over night to coagulate. The serum separates and may be pipetted off absolutely clear without cells. It is advisable to take the blood as far from a meal as possible,



as proximity to a meal makes the blood lipemic, interfering with perfect working conditions. (2) Having obtained 1 or 2 c.c. of clear serum, it is placed in a test-tube in the thermostat at  $56^{\circ}$  for one hour. Care must be taken not to permit the heat to rise too high (over  $58^{\circ}$ ). (3) After this, 0.2 c.c. is placed in each of two test-tubes, one the test, the other the control. (4) To each is now added 0.1 c.c. fresh complement. (5) To the test portion is added one unit of antigen. The control does not receive any antigen. (6) Each tube receives now 3 c.c. of a 0.95 per cent. NaCl solution. In order to be able to judge properly the correctness of the procedure, the more controls one has the better; it is therefore necessary to compare the serum to be tested with two sera from known positive and negative bloods. (7) Shake every tube well and place in incubator at  $37^{\circ}$  or  $38^{\circ}$  for one hour. During this time, if the serum is luetic the antibodies present will, together with the antigen, bind the complement and render it inactive for hemolysis. (8) After one hour incubation each tube receives two units of amboceptor and 1 c.c. of a 5 per cent. suspension of sheep cells in 0.95 NaCl. The tubes are again vigorously shaken and placed in the incubator at  $37^{\circ}$  and inspected after ten minutes. If the reagents are properly adjusted hemolysis begins in the control tubes in fifteen to twenty minutes, and careful watching becomes a very essential point at this stage of the test. As soon as the control is completely hemolyzed the tubes are to be compared; only those should be pronounced negative that show a transparent fluid the same as the control.

Permitting the tubes to stand undisturbed in a cool place ( $15^{\circ}$  to  $17^{\circ}$ ) for twenty-four hours shows in the positive test a deposit of red cells, the size of the deposit depending upon the severity of the infection or proximity to the initial lesion as well as upon the degree of balance of the reagents used. Usually a markedly positive serum gives at the end of twenty-four hours a clear supernatant fluid of a light pink hue with a bordeaux red accumulation on the bottom of the tube. The weaker the reaction, the redder the supernatant fluid and the scantier the deposit of cells. In testing more than one serum, the reaction in each individual test must be considered as finished as soon as the controls are completely hemolyzed, in which case the two tubes are immediately removed to a cool place.

**TECHNIQUE OF THE NOGUCHI REACTION.** *Principles Involved.* These are same as in the Wasserman, excepting that the amboceptor is directed against human cells, for reasons to be spoken of later. It also facilitates the handling of reagents, as they are mostly paper soaked in the antigen and amboceptor. These do not readily deteriorate, as is the case with fluid biological reagents. The serum does not need inactivation at  $56^{\circ}$ .

*Modus Operandi.* (1) With a capillary pipette allow one drop of fresh serum to fall into a narrow (1 c.m. lumen) test-tube. The pipette is not to be used for any other serum. (2) Add 0.05 c.c.

fresh complement. (3) To the front row (rear row for control) add one piece (more or less, depending on the titre) of antigen paper. (4) Prepare a suspension of human cells 1 drop of blood to 4 c.e. NaCl 0.95 per cent. It is best to prepare about 60 c.c. of NaCl solution and allow 15 drops of blood to fall from the experimenter's finger into the solution. The human cell suspension is placed over night in the ice box. Next morning the supernatant clear salt solution is pipetted off and a fresh quantity of NaCl is added (about 55 c.c.) to the cells in the beaker. Of this cell suspension add 1 c.c. to every tube in the rack. (5) Incubate for three-quarters or one hour at 38° or 39°, preferably in a large dish of warm water. Occasionally shake the tubes, to insure proper solution of the biological substance on the antigen paper. (6) Add to each tube (after incubation), front and back rows, one piece of amboceptor paper more or less, the quantity depending on the titre) and replace in the incubator, observing the result after ten minutes, and watching carefully the controls.

It will be noted in about fifteen minutes, more or less, that the rear row begins to get clear, and when complete transparency is obtained the test and control tube are to be removed to a cool place and observed. If the reaction is positive, then the front tube (test) will be opaque, in marked contrast to the control, which is transparent. For convenience of observation, I make use of a fine sealed tube (about 1 mm. in diameter) filled with black ink, which, when placed behind the control, will appear as a clear black line, whereas the positive tube will not show the black line, or it appears as a dim shadow—depending on the strength of the reaction.

It has been stated that a positive Noguchi test and a negative Wasserman is often due to the presence in the patient's serum of antisheep amboceptors. It is not necessary to perform this test with every serum as a control. Only sera giving the above results need be subjected to a verification. To demonstrate the antisheep amboceptor, place 1 c.c. of a 5 per cent. suspension of sheep cells in a test-tube, add 0.2 c.c. of patient's serum and 0.1 c.c. complement, add 3 c.c. of NaCl solution, place in incubator, and observe. If the amboceptor is present, the cells will dissolve and the mixture become transparent. The time consumed depends upon the number of amboceptor units present. I observed sera, capable of hemolyzing the cells completely in ten minutes.

**RATIONALE OF CONTROLS.** In the Wasserman and Noguchi reactions it is of vital importance to have every possible error excluded. For this purpose the controls used will answer. The substances to be controlled are the antigen, the amboceptor, and each individual serum.

*The Antigen Control.* This biological reagent, as is known, can per se inhibit hemolysis. To measure the degree of such interference, a tube containing a well-known normal serum (or, as I found just

as serviceable, no serum at all), plus antigen, plus complement, and antishoop amboceptor plus sheep cells ought to hemolyze in about twenty to thirty minutes. No reaction is to be considered as finished before the antigen control tube is completely hemolyzed.

*The Amboceptor Control.* Upon the efficiency of the antishoop amboceptor depends the rapidity of hemolysis of the sheep cells. It is therefore necessary to establish the amboceptor efficiency in a separate tube containing sheep cells, plus complement, plus antishoop amboceptor. It is not essential to add normal serum. The tube containing the above ingredients is always the first to hemolyze, requiring about fifteen to twenty minutes for a complete hemolysis.

*Control for Each Serum.* Every serum more or less has the power to interfere with hemolysis to a slight degree. In order to control the factor of individual inhibition, every serum tested is placed in each of two tubes, the front tube contains the antigen and all other biological reagents, the rear tube receives everything but the antigen. This shows the degree of individual inhibition as compared with the tube containing the amboceptor control.

*Efficiency of the Entire System.* For this a well-known luetic serum is utilized. The reaction is to be positive, and hemolysis should not occur in the front tube, even if exposed to incubation temperature for hours after the controls hemolyzed.

**EQUIPMENT.** At least one dozen or more of Mohr's pipettes, 1 c.c., graduated into  $\frac{1}{100}$ . One dozen 10 c.c. pipettes, graduated into  $\frac{1}{10}$ . One gross of ordinary test tubes. One gross of test-tubes 1 cm. in diameter, 12 cm. high. One-quarter dozen of graduated cylinders, 50 c.c.;  $\frac{1}{4}$  dozen 100 c.c. Two 50 c.c. measuring flasks with glass stoppers. A few pounds of glass tubing, 5 mm. bore, to make capillary pipettes. One-half dozen test-tube racks for Wasserman tubes;  $\frac{1}{2}$  dozen test-tube racks for Noguchi tubes. A piece of rubber tubing for tourniquet. One artery clamp for above. One dozen hypodermic needles, 19 bore. One thermostat regulated at 57° and one regulated at 37°. One electric centrifuge. Labels and pencil for writing on glass. One tall glass jar for flushing through used pipettes, height to be greater than any pipette used. One dozen Petri dishes. One dozen beakers, 100 c.c. capacity. Two fine forceps, and two Hagedorn needles. One package of quantitative filter paper. One razor (for killing guinea-pigs). One 15 c.c. Luer syringe.

**PREPARATION OF ANIMALS.** *Antishoop Amboceptors.* Several healthy rabbits (not less than four) receive every fifth day 1, 2, 3, 4, and 6 c.c. of well-washed sheep cells. This number of rabbits is used, as one or two may die during the injection weeks. The cells are obtained from the slaughter house and immediately defibrinated with a wire defibrinator or glass beads. In order thoroughly to wash the cells a high speed centrifuge is necessary, capable of making at least 3000 revolutions to the minute. Two of the cen-

trifuge tubes are filled with the fluid sheep blood, it being advisable, in order not to spoil the centrifuge, to have them of equal weight. The first centrifugalization brings the cells to the bottom, and the clear supernatant serum is pipetted off. The cells are now mixed with 0.95 per cent. NaCl solution and centrifugalized again, and the supernatant clear fluid is again pipetted off; this is repeated three times. The cells are now approximately serum-free. The entire quantity of cells in the tube is now brought up to its original volume with 0.95 per cent. NaCl solution, and of this, 2 c.c. is used for the first injection. With a sterile glass syringe this quantity is injected into the peritoneal cavity, having previously shaved and cleaned the puncture area. Cotton and collodion prevent wound infection. This procedure is repeated five days later with 4 c.c. of cells brought to its original volume, etc., until each animal has been injected five times. Nine days having elapsed since the fifth injection, the serum of the rabbit contains now a high lytic power against the red blood corpuscles of the sheep. The rabbit is killed and its serum used.

In the Wasserman reaction 1 c.c. of a 5 per cent. suspension of well-washed sheep red cells in 0.95 per cent. NaCl solution is the standard dose for each test. It is evident, therefore, that in order to test the power of our rabbit serum (antisheep amboceptor, as it is now called) we must use this quantity of sheep cells. Into each of six test-tubes is placed 1 c.c. of a 5 per cent. suspension of sheep cells in NaCl 0.95 per cent. These are marked from 1 to 6, and to each is added 0.1 c.c. of fresh guinea-pig serum (this is known as the complement serum and is the quantity used in the Wasserman test). We now add to test-tube (1) 1 c.c. of a 1 to 200 solution of our amboceptor. To test-tube (2) we add 1 c.c. of 1 to 400; to test-tube (3), 1 c.c. of 1 to 800; to test-tube (4), 1 c.c. of 1 to 1600; to test-tube (5), 1 c.c. of 1 to 3200. This is placed into the thermostat at 37° and the result noticed after fifteen minutes, thirty minutes, up to two hours. It will be seen that in fifteen minutes test-tube (1) is clearing up, or is clear (hemolysis); this would indicate that 1 c.c. of a 1 to 200 solution of our amboceptor is capable of destroying in fifteen minutes 1 c.c. of a 5 per cent. suspension of sheep cells. This proportion—1 to 200—is too strong, and may give negative results with some positive sera. The unit strength of the antisheep amboceptor is usually twice the quantity capable of hemolyzing the 1 c.c. of cells in two hours. If 1 to 1600 shows hemolysis after two hours and 1 to 3200 does not, then 1600 divided by 2 is the strength of the amboceptor, one unit equals 1 to 800. It is best to run two series of titration—one like the above, the second beginning with 1 to 250, 1 to 500, 1 to 1000, etc., so that a proper mean can be established and a more exact unit made. In table form the above is expressed as follows:

		Sheep cells.		Cells hemolyzed in
		5% 1 c.c.		
Tube 1 amboceptor = 1 to 200	Complement 0.1			15 minutes.
" 2 " = 1 to 400	" 0.1	" "		30 minutes.
" 3 " = 1 to 800	" 0.1	" "		50 minutes.
" 4 " = 1 to 1600	" 0.1	" "		1½ hours.
" 5 " = 1 to 3200	" 0.1	" "		2 hours.

Strength of 1 unit, 1 to 1600; dose for 1 test, 1 to 800. Date.....

A full-grown rabbit usually furnishes from 50 to 60 c.c. of serum. This is to be kept in a glass-stoppered flask in the ice box (lower compartment). The hemolytic power does not indefinitely remain the same as in the beginning; it is, therefore, necessary to establish the titre at least once every week, and to make up the dilutions accordingly. These dilutions are to be prepared on the day of testing. The rabbit serum does not have to be inactivated to get rid of the complement in it, as the quantity of serum used is too small to influence in any way the resulting outcome of the test.

*Preparation of Complement.* A full-grown guinea-pig is held over a Petri dish, and after having it narcotized, the bloodvessels of the neck are severed with a razor. Suspended by the hind legs the animal is exsanguinated, and the collected blood is permitted to remain at room temperature for at least three hours. The serum collects in large drops and may be pipetted off, or the coagulum plus the serum is placed in a centrifuge tube and after five minutes centrifugalization the supernatant serum is pipetted off into a sterile test-tube; but such a serum is not as reliable as when left for three hours with its cells. About 6 c.c. of complement is obtained from one guinea-pig.

*Preparation of Sheep Cells.* Obtained from the slaughter house, the cells are washed three times with 0.95 per cent. NaCl solution, and 1 or 2 c.c. is mixed with 20 or 40 c.c. of salt solution, making a 5 per cent. suspension of cells.

*Preparation of Antigen.* The fresh liver of a luetic foetus or the liver of any baby cadaver is chopped up very finely, and the mass is spread on a few Petri dishes and dried. The drying process is hastened by a current of air produced by an ordinary electric fan. Lately, not only baby livers, but also the livers of dogs, the hearts of guinea-pigs, and other organs were used to make antigen. The usefulness of the antigen is only established when in actual standardization it is found serviceable and works faultlessly with decidedly syphilitic and unquestionably normal sera. Consequently it makes little difference whether one uses the extract obtained from the liver of a syphilitic foetus or from the heart of a guinea-pig, provided they are well titrated.

It is better—according to German workers—to use more than one extract, and have a series with well standardized luetic liver antigen,

one with guinea-pig heart, and another with dog liver, or normal human liver. To proceed with the making of antigen the obtained dried liver is rubbed into a powder and kept in an exsiccator over  $\text{CaCl}_2$  in a cool, dark place. According to Tschernogubow, such a powder is serviceable for a very long time. Of this powder, 0.5 gram is extracted at room temperature or in an ice box with 25 c.c. of 95 per cent. alcohol for twenty hours, then filtered, and the filtrate used for experiments.

For the actual Wasserman test, one part of this opalescent filtrate is diluted with five parts of 0.95 per cent.  $\text{NaCl}$ , and 0.5 to 1 c.c. used for each test-tube, the dose depending upon the established titre. The above process extracts from the liver substances soluble in alcohol, chiefly bodies of a fatty nature (lipoids). There are other means of obtaining lipoids, the above being one of the simplest, having also in view the preservation of the antigen in an active form. The liver, instead of being dried and powdered, may be directly extracted with five volumes of absolute alcohol, and the extract obtained by driving the alcohol off at a temperature not higher than  $40^\circ \text{C}$ . or with the electric fan. The obtained extract is much more powerful than the above, is soluble in ether, from which  $\text{NaCl}$  solutions are made for use. The titre is established carefully as follows:

*Titration of Antigen.* The unit dose of antigen must be of such a strength that one unit will completely inhibit hemolysis of 1 c.c. of a 5 per cent. suspension of sheep cells, with 0.2 c.c. of a known luetic serum plus 0.1 c.c. of complement; provided double this dose does not interfere with the complete hemolysis of cells using a known normal serum and complement.

TABLE OF ANTIGEN STANDARDIZATION.

Luetic Series.				Normal Series.			
Each tube contains syphilitic serum, 0.2; complement, 0.1; cells, 1 c.c. 5%; amboceptor, 2 units.				Each tube contains normal serum 0.2, complement, 0.1; cells, 1 c.c., 5%; amboceptor, 2 units.			
				Hemolysis.			
Tube 1, Antigen, 0.025		1 hour 15 min.		Antigen, 0.025		15 minutes.	
" 2, " 0.05		1 " 25 "		" 0.05		15 "	
" 3, " 0.075		2 " 50 "		" 0.75		15 "	
" 4, " 0.10	} No hemolysis after 24 hours in incubator.			" 0.10		20 "	
" 5, " 0.15				" 0.15		30 "	
" 6, " 0.20				" 0.20		35 "	

Dose of one unit, 0.1 c.c.

From the above facts it is evident that the dose next to the largest hemolyzing dose is the strength of one unit, or 0.1 c.c. It is also apparent that 0.2 c.c., or a double dose, will not inhibit hemolysis when used with a normal serum.

In establishing the unit dose of antigen as well as antisheep

amboceptor it is of utmost importance to titrate two or three times in order to get as uniform results as possible, and only uniform work will enable one to come to a proper conclusion as to which is the necessary dose. For establishing the strength of the antigen and amboceptor, well-known fresh luetic and normal sera are to be used, as well as fresh suspension of cells and fresh complement.

Before using the standardized reagents it is advisable to perform two or three actual tests with well-known positive and negative sera. After this the substances may be considered safe for use. The above lines will give one a fair idea concerning the preparation of the biological reagents for the Wasserman reaction. For the Noguchi reaction it will be necessary, first, to acquaint the reader with the principles involved, and then the preparation of reagents will follow.

**PRINCIPLES OF THE NOGUCHI TEST.** Workers with the Wasserman reaction often could not explain why a positive result could not be obtained with some true luetic sera. Later it was demonstrated that this was due to the presence in the human serum of substances capable of dissolving the red blood corpuscles of the sheep; in other words, some human sera contained antisheep amboceptors. From an analysis of the workings of the Wasserman test, one could offer an objection to the statement by pointing out the fact that even in the presence of natural antisheep amboceptors, there would be no complement to bring about lysis in the hemolytic system, for the complement has been bound up in a luetic serum by the antigen. This is certainly true to some extent, but it is also true that in the presence of an excess of amboceptors, a very small quantity of unbound complement will suffice to bring about complete solution of the sheep cells used in the test. Now we very well know that in performing the Wasserman reaction we are dealing with an unknown quantity, this unknown quantity being the number of syphilitic antibody units (or some substance capable of binding complement with the antigen) present in the luetic serum. It needs no comment that the stronger and more virulent the infection, the greater the number of such bodies in the serum and naturally the firmer and more complete the binding of the complement. Sometimes the quantity of antibody is so small that a goodly portion of the complement escapes unbound and does its work by bringing about partial hemolysis; this is the condition of affairs taking place in some weak reactions. If such a serum contained antisheep amboceptors, they would have enough complement to cause hemolysis and render the result negative.

An old experiment of Ehrlich and Morgenroth proves that the greater the number of amboceptor units, the smaller the quantity of complement necessary to bring about complete hemolysis. If the patient's serum contain 10 or 20 units of antisheep amboceptor, and if only  $\frac{1}{10}$  or  $\frac{1}{20}$  of a unit of complement escapes deviation, this

quantity will prove amply sufficient to cause hemolysis. In the Noguchi test this cannot take place, for the hemolytic system used consists of human cells plus antihuman amboceptor, and, naturally, the human organism does not contain antihuman amboceptors. Luetic sera containing antisheep amboceptors will give a negative Wasserman but a positive Noguchi test.

**PREPARATION OF REAGENTS. *Antihuman Amboceptor.*** Rabbits are injected with human cells the same as the sheep rabbits. After nine days the rabbits are killed, their serum collected and disposed of as follows: The fluid amboceptor loses strength on standing, so much so that it may not contain one-fourth of its original power a month after the first titration. In a dry state it can be used for a very long time without losing its strength. I prepare my antihuman amboceptor by cutting quantitative filter paper in 5 mm. squares. These squares are stuck on to pins fastened to a cardboard. With a very fine capillary pipette (as fine as one as can be made) one drop is blown on each piece of filter paper and placed in the thermostat for drying. In half an hour the papers are dry and fit for use. By this method each square receives exactly the same quantity of serum, and is not subject to differences in dissemination which must be considered when the serum is blown on a larger piece of filter paper and cut subsequently in 5 mm. squares. My method takes longer, but the difference is worth while, for each square holds exactly the same quantity of amboceptor. My present amboceptor is two and one-half months old and as good as new. In my work I find one piece of this amboceptor serviceable.

TITRATION OF ANTIHUMAN AMBOCEPTORS.

	Human cells 1 drop to 4 c.c. NaCl.	Complement.	Hemolysis in
Tube 1, Amboceptor, $\frac{1}{2}$ piece	1 c.c.	0.05	2 hours.
" 2 " 1 "	1 c.c.	0.05	20 "
" 3 " $1\frac{1}{2}$ "	1 c.c.	0.05	11 "
" 4 " 2 "	1 c.c.	0.05	8 "

As a result of five months' work with the Wasserman and Noguchi tests, I am enabled by this time to give a fair opinion as to its uses. Shortly stated, the two reactions are to my mind of the foremost importance to the clinician, and so far as accuracy is concerned, they almost occupy the first place among our means of detecting disease. The above statement is not at all to be marked as enthusiastic, for I must admit that six or eight weeks of work was spent on a very rough road to overcoming difficulties and getting acquainted with the peculiarities of the reaction, differences in the bloods submitted for tests, changes in the biological reagents, etc. My first



300 tests contained about 30 per cent. error, which by steadfast application and constant research into the causes for these mistakes, enabled me to weed them out to such an extent that now, after five months' work, I am in a position to report in 100 luetic sera, 98 to 99 positive results. In the following lines will be given the means of arriving at such a degree of precision.

First, no one who has worked with the Wasserman reaction alone has a right to claim infallibility. This is especially true for the first two months of work. Constant application and undivided attention are the prerequisites for thoroughness, and only such workers are to be depended upon for their results. I believe it to be almost impossible to arrive at a high degree of technical skill without the above conditions. The handling of pipettes, even by laboratory workers, has to be improved and rendered faultlessly exact, for a drop more or less may sometimes mean a false diagnosis. As to the use of the Wasserman test alone, without the Noguchi modification, I would consider as lacking in proper controls, for, as stated before, the Noguchi modification eliminates the possibility of a negative result when antishoop amboceptors are present; and permit me to emphasize that they are present quite frequently, being the *raison d'être* of negative results in about 8 or 9 per cent. of Wasserman tests with luetic sera. Using the Noguchi test with the Wasserman places one on a much surer footing, and not only gives one better results, but also enables the worker to detect inaccuracies in the biological reagents used in the Wasserman tests.

As mentioned before, the Wasserman reaction gave a negative result in 8 or 9 per cent. of syphilitic sera. This rather undesirably high percentage of error was reduced to 1 or 1.5 per cent. when using the Noguchi and the Wasserman combined. It became apparent from the first 100 or 150 reactions that the Noguchi test, besides giving a positive reaction with all luetic sera (99 times out of 100), will sometimes give a positive reaction with a negative serum, and this to an extent of 7 per cent. As alarming as such a high degree of inaccuracy may at first sight appear, it becomes irrelevant when used with the Wasserman reaction. I have formulated a system of recording the results, which, at a glance, will give the proper interpretation of the findings in the two methods. The table is an outcome of 1400 reactions, and with it 98.2 of correct interpretations were obtained. Let me impress upon the worker the necessity for more than one test on each patient. I never render a decision after one test. Always perform two Wasserman and two Noguchi tests on different days, using the same serum. It is also to be borne in mind that a fairly marked Wasserman reaction, 99 times out of 100, means syphilis, and that a negative Noguchi the same number of times means no syphilis. The two methods are very decisive, but in opposite ways; and used together, carry with them an assurance which no amount of thoroughness and precision

will replace if only one method is used. I, therefore, recommend, and am sure will be supported by other workers, that the Wasserman reaction is much less conclusive when performed without the Noguchi test, and that in the combination of the two methods we really possess a very valuable diagnostic aid.

TABLE OF INTERPRETATION OF RESULTS.

	Wasserman test first day.	Noguchi test first day.	Wasserman test second day.	Noguchi test second day.	Opinion formed.
1	S +	S +	S +	S +	Unquestionably syphilitic.
2	+	+	+	+	Unquestionably syphilitic.
3	+	—	+	—	This happens rarely, and if technique is correct, means positive. Should be done three times.
4	—	+	—	+	If antisheep amboceptors are present = positive; if no antisheep amboceptors are present = negative. Should be done three times.
5	—	W +	—	+	Suspicious. Must be decided clinically
6	—	W +	W +	W +	Positive, but weak.
7	—	S +	—	S +	Some fault with the reagents in Wasserman test, unless antisheep amboceptors are demonstrated, then positive.
8	W +	+	—	W +	= positive.
9	—	W +	—	W +	= negative, even if antishcep amboceptors are demonstrable.
10	—	+	—	—	= negative.
11	—	—	W +	+	Faulty technique. Repeat twice.
12	W +	W +	—	—	= negative. Repeat.

S + = strongly positive.  
W + = weakly positive.

+ = ordinary reaction.  
— = negative.

The above table is compiled from numerous actual observations, and is not influenced by the personal equation of the worker. To eliminate this factor, I have performed the last few hundred tests without a knowledge of the patient's condition. In many instances the test-tubes with the patient's blood were given me bearing only a number for identification, and only after rendition of the final result was the clinical diagnosis revealed to me. On one such occasion 12 sera out of 18 reacted positively, and proved to be from 11 cases of tabes and one of tricuspid stenosis. The latter subsequently reacted ten times positively. Such non-knowledge of the patient's condition is to be recommended if one wishes unbiased results; and statistics obtained by such means are far more valuable than those obtained by giving the laboratory worker the diagnosis with the blood. The clinical findings belong to the doctor, and ought to be offered in exchange for the laboratory report, and not sooner.

This work comprises results from 1390 analyses. The first 300

are unreliable on account of lack of technique. The remaining 1090 carry with them a high degree of precision. Analyzing the sensitiveness of each method independently, I find that out of 503 sera examined by the Noguchi method, 43 were contrary to the diagnosis of expert clinicians. Of these 43 probably incorrect results, 35 were interpreted as positive and 8 as negative. The Wasserman reaction behaved as follows: Out of 487 sera, 37 were wrong. Of these 37, 30 were negative and 7 positive. Using the combined method of reading results—having performed two Wasserman and two Noguchi tests and then rendering a report—the results were as follows: Out of 487 reports, 9 were contrary to the clinical picture; of these, 5 were negative and 4 positive, making it less than 2 per cent. error.

Before giving my conclusions, I would like to offer a few explanations of the peculiarities and at times perplexing results obtained while working with complement deviation. On more than one occasion the presence of antishoop amboceptors has been blamed for a negative Wasserman reaction. This is true only to a certain extent, for we know that in the presence of a sufficient quantity of syphilitic antibody, a perfect and complete deviation of complement will take place with a well-standardized antigen. The antishoop amboceptor comes into prominence only when there is a paucity in luetic antibody, and then only will render the Wasserman reaction useless.

Some guinea-pigs furnish a serum which is very poor in complement, rendering the amboceptor powerless or too weak to hemolyze the given quantity of cells; in such a case the outcome is a weak positive reaction in a negative serum.

The sheep cells must also be considered, as they, too, have varying powers of resistance to the amboceptor, and will sometimes remain intact for hours. This is one of the reasons why some controls and tests react very sluggishly. Another reason for a prolonged resistance to the amboceptor is the presence in the patient's serum of anticomplemental substances which hinder or render inert the completing function of the complement. In such a case the addition of another half dose of guinea-pig serum will bring out clearly the nature of the serum, and also decide its luetic or negative qualities.

Although the above deviations cause delay, puzzle and discourage the beginner, by far the greatest source of error lies in the worker himself, especially when a drop more or less is considered as insignificant, or any pipette as clean enough. Thorough cleanliness, using sterile dry pipettes and containers, as well as faultless pipetting, are conditions *sine qua non* in the performance of the Wasserman and Noguchi tests; they are only acquired after weeks of constant work and application. I do not wish by these statements to discourage anybody from working with the methods, but I would advise the worker not to place himself on record before every detail

has been mastered and he is able to answer why and wherefore certain tests were negative on one occasion and again positive on another day, and which of the two is correct. The laboratory worker, being responsible to the clinician for his statements, ought to be in a position to help him considerably, but only when his work has been carried out very carefully, unbiassed by personal opinion, and submitting the result of a delicate test as read from the test-tube. I do not believe we are as yet in a position to say that a serum preventing the hemolysis of sheep cells in the Wasserman test, or human cells in the Noguchi modification, means the presence of syphilis. Leprosy gives it, trypanosomiasis is reported to give the reaction, and undoubtedly, there are other conditions which give rise to the formation of substances in a patient's serum which, when brought in contact with antigen (lipoid bodies), are capable of inhibiting, destroying, or deviating the completing action of the complement, so that hemolysis will not take place when a specific hemolysin and cells are placed in such a mixture. I had occasion to analyze two cases of scleroderma, and found in both the reaction positive. Whatever the process may be, the explanation of its *modus operandi* is still a theory made to fit the well-known exposition of Ehrlich's concerned in immune processes, which in itself is only an ingenious theory. The practical man wants a reliable report on the blood submitted for analysis. In my case, only yes or no was accepted. I was confronted with questions as to the significance of a weak reaction, an ordinary and a strong reaction. From the above remarks it is apparent that one is hardly justified to state positively that even a strong reaction signifies, without the least doubt, syphilis. In the vast majority of bloods syphilis is most likely the cause for a strong reaction, but it need not at the same time be the only factor responsible for its appearance.

A strong reaction naturally carries with it a greater degree of assurance in rendering a decision than a weak reaction. This is especially true of the Wasserman test, for at no time was a strong reaction obtained with this method unless the blood came from a patient giving clinically or anamnestically signs of syphilis. A strong positive reaction with the Noguchi test is much less significant, at least in my experience. I obtained positive results with the Noguchi method when, from the physical examination and the history, syphilis could be excluded to the satisfaction of the clinician. On the other hand, a distinctly negative result, using the Noguchi method, is very valuable, and in the majority of instances comes from an individual free from a syphilitic taint, as corroborated subsequently by a careful examination.

In the above work no deviation from the accepted technique was resorted to. In the Noguchi tests personal communication with the originator of the method greatly facilitated the progress of my work by rendering clear some obscure phenomena and furnishing a re-

liable antigen. The amboceptor I prepare myself by a slightly different method, the aim being greater uniformity in the 5 mm. squares of paper used in the tests. In every other detail the technique is exactly as advocated by Dr. Noguchi, using the same reagents, and working with the same controls.

CONCLUSIONS. 1. Every beginner, for the first month or two, will obtain unsatisfactory results from lack of proper technique.

2. Having mastered the technical difficulties, always perform another test for verification.

3. Acquire the habit of working with two methods, the Wasserman and Noguchi.

4. Every week or ten days, spend a day in standardizing reagents.

5. With proper technique and well balanced reagents it is possible to report correctly in 98 per cent. of cases.

6. Questionable reactions are not to be used for diagnosis, and if a given serum does not react strongly after a number of repetitions of the tests, the diagnosis is to be left to the clinician.

7. I find that the Wasserman reaction gives negative results in about 7 per cent. of positive sera, treatment periods excluded.

8. The Noguchi method gives 8 per cent. of positive results in clinically well-established non-syphilitic individuals. The positive reactions in these cases are ordinary reactions, and cannot be said to be remarkably strong.

9. Exceptionally strong reactions are obtained in untreated cases of general paresis with both tests, as well as in primary sores four weeks after infection.

10. With time, the antibody content of the serum diminishes. The antibody content also diminishes during inactivation to about one-third. (Personal communication by Dr. Noguchi.)

11. The table of interpretation of results was of great help in rendering many correct reports, and served to some extent as a guide in the disposal of the serum submitted for testing.

12. The compilation of this table took place after analyzing the results from 1390 reactions.

13. I do not feel justified to place myself on record concerning the specific or non-specific nature of certain diseases. However, the majority of sera from tabetics (78 per cent.) and most sera from general paretics (not treated recently) deviate complement, and the latter most strongly. In diabetics a positive result could rarely be had. The few cases of aneurysm and aortic lesions as well as one case of tricuspid stenosis, all gave a positive result. Out of 84 locomotor ataxia cases, 66 gave a positive Wasserman and 70 a positive Noguchi reaction. The findings in clinical conditions will be the subject of another communication.

14. I am not at present in a position to state the influence of treatment on the reaction, and to what extent or manner my method of interpretation will be influenced.

I wish to thank all gentlemen who were helpful in furnishing material for work, my gratitude being due to Dr. I. Abrahamson for initiating this work in the Montefiore Home Laboratory, to Dr. Noguchi for his generous help in elucidating complex phenomena and furnishing some reagents, and to Drs. H. Brooks and S. Wachsmann for encouraging and facilitating the research.

## A STUDY OF THE ALLEGED PRESENCE OF TUBERCLE BACILLI IN THE CIRCULATING BLOOD.

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TWELVE months have now elapsed since Rosenberger<sup>1</sup> read his initial paper before the Pathological Society of Philadelphia, upon the presence of tubercle bacilli in the blood. This paper gave rise to considerable enthusiasm in local medical circles and no little interest to the medical world at large, because he asserted that it was easily possible to demonstrate the presence of tubercle bacilli in the blood of every case of tuberculosis, by means of a technique so simple that it became a matter of surprise that previous efforts, along this same line, by many competent investigators, should not long ago have been rewarded with equal success. Many accepted his findings quite readily, while others listened to them with a good deal of reservation.

Rosenberger's original studies comprised 50 cases divided as follows: 2 cases of fibroid tuberculosis; 1 case of pneumothorax; fifteen cases of incipient tuberculosis; 23 cases of advanced tuberculosis, and 3 cases of the laryngeal form of the disease. He has since augmented this number, so that at the present time they embrace over 300 observations, including cases of lupus. In all of these cases he has met with the same success, finding the bacillus in the blood in every instance.

This contribution was immensely important, because, if correct, some of our preconceived ideas concerning tuberculosis must be modified, and because it would afford the clinician a simple and almost infallible means of diagnosing the malady in its earliest incipency, a matter at the present time perplexing and difficult, if not impossible. In lieu of all this it is astonishing to find that, with the exception of two brief contributions on the subject, Rosenberger's observations have not been confirmed.

In reviewing the literature in the chronological order in which

the reports have appeared, the following are noted: Forsyth<sup>2</sup> reports the study of 12 cases, with positive results in 10. Burnham<sup>3</sup> and Lyons<sup>3</sup> detailed their observations in 10 cases—negative in every instance. Schroeder and Cotton<sup>4</sup> published the results of their studies of the blood of 48 tuberculous cattle, with findings uniformly negative. Mohler,<sup>5</sup> carrying on an independent investigation, examined the blood of eight tuberculous cattle with negative results. Ravenel and Smith<sup>6</sup> state that they have examined the blood of 18 cases, and have been unable to demonstrate tubercle bacilli in any of them. Petty and Mendenhall<sup>7</sup> studied 10 cases, only 7 of which were tuberculous, and in all of them bacilli were demonstrable in the blood. One case of axillary adenitis, presumably tuberculous in nature, but subsequently shown by the pathologist to be sarcomatous, gave a negative result. The two remaining cases, it is to be inferred, were cases of enteric fever; but in both of them acid-fast organisms supposed to be tubercle bacilli were found in the blood.

Hewat and Sutherland<sup>8</sup> made twenty-two examinations of twenty tuberculous individuals, and in one case only were they able to demonstrate acid-fast organisms. However, in repeating the examination of the patient's blood in which two acid-fast were found in the initial test, it was negative, which led the authors to believe that the presence of the organisms was due to incidental contamination. Anderson<sup>9</sup> examined the blood of 48 cases of human tuberculosis together with 13 guinea-pigs and 8 rabbits experimentally infected by the Rosenberger method. Of these, but one, a case of human tuberculosis, revealed acid-fast organisms in the blood specimen; but inasmuch as guinea-pig inoculation was negative, Anderson does not think that the organisms found were tubercle bacilli. It is of interest to note that in 3 of the rabbits cultures were successfully grown from the blood, and this in face of the fact that it was impossible to demonstrate the organisms by smear in the blood of these animals.

In this preliminary report is added a study of 56 cases, in the blood of which tubercle bacilli were sought with the utmost pains. The cases were divided as follows: Five cases of suspected tuberculosis in which the physical examination was negative or questionable; 10 cases in which physical examination was clearly positive, but in which the sputum was either negative or was not examined; 4 incipient cases in which both the physical examination and the sputum were conclusive; 9 cases moderately advanced; 1 moderately advanced case complicated with laryngeal tuberculosis; 1 case of

<sup>2</sup> Brit. Med. Jour., 1909, i, 1001.

<sup>3</sup> Jour. Amer. Med. Assoc., 1909, liii, 731.

<sup>4</sup> Bulletin No. 116, U. S. Department of Agriculture.

<sup>5</sup> Ibid.

<sup>6</sup> Jour. Amer. Med. Assoc., 1909, liii, 649.

<sup>7</sup> Ibid., 1909, liii, 867.

<sup>8</sup> Brit. Med. Jour., October 16, 1909.

<sup>9</sup> Bulletin No. 57, Hygienic Laboratory, United States P. H. and M. H. S.

tuberculous adenitis; 1 case of miliary tuberculosis in an infant; 1 case of bilateral senile pneumonia; and lastly, 2 cases of epidemic cerebrospinal meningitis.

Particular interest was aroused through the appearance of Rosenberger's paper, because before its appearance a similar independent investigation was in progress at the Henry Phipps Institute, the technique employed differing but little from that of Rosenberger. The work had been abandoned, however, after the careful study of the blood of 8 cases of undoubted tuberculosis was productive of negative results only. The technique was as follows: 5 c.c. of blood was withdrawn from any convenient vein and immediately added to an equal quantity of a 2 per cent. solution of sodium citrate. The mixture was then centrifugalized for ten minutes in a rapidly revolving electric machine, the supernatant fluid pipetted off, distilled water added to the sediment, the mixture vigorously shaken and recentrifugalized. The sediment thus laked was withdrawn with a pipette, thick smears made on clean glass slides, fixed, and stained for five minutes in carbol fuchsin, decolorized in 5 per cent. nitric acid in 95 per cent. alcohol, and counterstained for five seconds in borated methylene blue. Rosenberger at first employed the centrifuge but subsequently discontinued its use, as he thought it gave less satisfactory results than simple sedimentation. On the other hand, Forsyth employed the centrifuge, which in his hands gave better results.

Rosenberger's technique as given in his original article, was rigidly followed in my latest series of cases. It requires that the blood, after being drawn and agitated with a citrate solution, be allowed to sediment for twenty-four hours in a refrigerator, at the end of which time the sediment is pipetted off and thickly spread upon clean glass slides, which are then placed on a copper plate and subjected to a low degree of heat until dry. They are subsequently laked by placing them in a jar of distilled water and the resulting thin, almost colorless film dried and fixed by rapidly passing through a Bunsen flame. They were next stained, carbol-fuchsin with Pappenheim's stain as a decolorizer and counterstain being employed. In the first fifteen examinations this technique was employed exactly, but Pappenheim's solution was eventually discarded because it gave rise to so many confusing artefacts. Indeed, in a large majority of the slides so stained these were met with and were sometimes so deceptive in their resemblance to tubercle bacilli that co-workers in the laboratory who were asked to examine them frequently differed in their judgment. The fact, however, that after the Pappenheim stain was abandoned, and decolorization in acid alcohol with counterstaining in borated blue substituted for it, no such bodies were encountered would, I think, seem to prove that they were artefacts.

In the initial part of the investigation six slides were made from



the blood of each case and each examined critically field by field, but after 7 cases had been so studied it was deemed sufficient that two slides be prepared, and from thirty minutes to three hours devoted to a study of each of them. Singularly enough, in the few cases in which acid-fast organisms were demonstrable they were found in less than fifteen minutes. In one case only three minutes were required, in another it required only eight minutes' search to discover the first group of bacilli, and a second group was discovered on the same slide after twelve more minutes. In studying another slide, only thirteen minutes were required to find a group of organisms, which were the only ones met with, although another half hour was expended in attempting to locate more. Bacilli were found in six minutes in another case, and a few others after twenty-three more minutes. Lastly, one and a half minutes was all the time required to demonstrate them in another case.

The cases which gave positive results were five in number, and, remarkable though it may seem, with two exceptions were not cases of tuberculosis. As a matter of fact, if the case of miliary tuberculosis in the infant and one suspicious case of incipient tuberculosis be excluded, every case of tuberculosis examined gave a uniformly negative result.

The 5 cases referred to as being positive were as follows: One case of miliary tuberculosis; 1 case of suspected incipient tuberculosis; 1 case of senile bilateral pneumonia; and 2 cases of epidemic cerebrospinal meningitis. The finding of acid-fast organisms in the blood of the cases of cerebrospinal meningitis was of so much interest that it may not be amiss to enter a little into detail regarding them, because it proves how readily the clinician could be—and was for a time—led astray in his diagnosis by such laboratory findings.

CASE I.—W. B., a student in one of the colleges of the suburbs of Philadelphia was admitted to the Bryn Mawr Hospital with a history of headache and malaise for three or four days prior to admission. The headache was very intense, pyrexia was present, the pupils were dilated, and he complained of some abdominal pain. At times he talked incoherently. His neck was very slightly rigid, with no pain on movement. There was anesthesia of the cornea. No rose spots were demonstrable. The attending physician suspected enteric fever, although a tentative diagnosis of meningitis was made. A Widal test was negative, and a leukocyte count of 10,200 was obtained. A lumbar puncture being refused, 10 c.c. of blood was withdrawn from an arm vein, 5 c.c. of which was utilized in making a blood culture for the purpose of demonstrating typhoid bacilli if possible, the other 5 c.c. being mixed with a citrate solution to be examined for tubercle bacilli. On the following day the patient's symptoms had become intensified. He was now delirious, there was marked rigidity of the neck, and herpes labialis

appeared. Lumbar puncture was still refused. Examination of the blood on this day showed acid-fast bacilli, and in the absence of any epidemic of cerebrospinal fever, a diagnosis of tuberculous meningitis with miliary tuberculosis was made.

CASE II.—P. B., a college chum and room-mate of W. B., was admitted to the same hospital on the day that the diagnosis of Case I was supposed to have been cleared up. He also had marked meningitic symptoms—delirium, retraction of the neck, and the characteristic decubitus assumed by such victims. Kernig's sign was marked. Becoming ill so soon after his room-mate and with similar symptoms, it was suspected that both young men were the victims of the epidemic form of cerebrospinal meningitis, and a lumbar puncture was performed. The fluid obtained was purulent, and upon microscopic examination showed innumerable diplococci with the morphological and tinctorial characteristics of the meningococcus. No acid-fast bacilli were found, though they were carefully searched for. A lumbar puncture was now done in Case I, and meningococci were also found, but again no acid-fast bacilli could be discovered in the spinal fluid. As a matter of interest, 5 c.c. of blood from Case II was secured and examined for tubercle bacilli, and to the writer's surprise a few acid-fast organisms were demonstrated.

True, there is a possibility that both of these patients were tuberculous, though it must be admitted that it would be a peculiar coincidence. We must also remember that Rosenberger claims to have demonstrated acid-fast bacilli in the blood of apparently healthy individuals. Might the blood of these two individuals have revealed acid fast bacilli had such an examination been made prior to their falling ill? Petty and Mendenhall found acid-fast bacilli in the blood of two of their patients who were apparently suffering from typhoid fever. Be that as it may, the point is, that even though acid-fast bacilli were demonstrable in the blood, it could scarcely be regarded as definite proof of the existence of tuberculosis. Had Case II not contracted the disease, W. B., dying as he did after a protracted illness, would have been considered a case of tuberculous meningitis with miliary tuberculosis, and a death certificate issued accordingly, when, as a matter of fact, he was not a victim of either disease. P. B. died also, and it might be added that an autopsy, though urgently sought for, was refused in both instances. No postmortem examination was, unfortunately, permitted in the case of bilateral pneumonia, in whose blood acid-fast organisms were found. The patient was a woman, aged sixty-five years, whose clinical symptoms were characteristic. Repeated examinations of the sputum never showed the presence of tubercle bacilli, though pneumococci were found in abundance.

The 50 cases of tuberculosis, the study of which form the basis of this paper, were ward and dispensary patients at the Henry

Phipps Institute of Philadelphia. In every case the blood was secured by introducing a needle into a vein, and the staining performed according to the technique already given. Careful examinations were made, and with a single exception were uniformly negative. The one patient in whose blood acid-fast organisms were found presented no physical signs whatsoever, though her history was suspicious. Two separate groups, one of five and one of three acid-fast organisms, were found in the blood of this case. They were not typical for the tubercle bacillus. In fact, in no case have the organisms discovered been morphologically typical. In some instances they appeared much larger and broader with round ends and a pale pink color; in other instances they were short and stained intensely. None showed irregularity of staining, and in no case was clumping observed. The bacilli found in the case of W. B. were chiefly of the large, broad type, and peculiar in that one group of the organisms were in chain formation, two chains lying parallel, one consisting of five elements, the other of four.

**INOCULATION EXPERIMENTS.** In order that the character of the organisms might be more accurately investigated, inoculations of guinea-pigs with the blood was used as a control. Approximately 2 c.c. of the blood from each of 37 of the 50 cases of tuberculosis was inoculated into guinea-pigs. In the first 21 animals the injection was made intraperitoneally, but as it was suggested that the peritoneal fluids might possibly exert some bactericidal influence, the subcutaneous method was substituted for the remainder. Two pigs were inoculated from each case, 74 animals being thus utilized; 17 died prematurely—under three weeks. Of the remainder, 13 survived the injection from two to seven months; 14 from from one to two months, and 5 approximately three weeks. All were carefully autopsied, and in no single case was there any macroscopic evidence of tuberculosis, glandular or otherwise. The failure to induce the disease in guinea-pigs by injecting them with the blood from tuberculous individuals is supposed by Rosenberger to depend upon the attenuation or death of the organisms in the blood stream. The experiments of Liebermeister<sup>10</sup> are, however, convincingly opposed to this view.

**SOURCES OF ERROR.** That Rosenberger should report constant positive results in a large series of cases, and that Ravenel and Smith, Cotton and Schroeder, and Mohler uniformly negative ones, and that negative results should occur in the 50 cases herein reported, is, to say the least, extremely perplexing. To say that the organisms are only present in the blood at certain stages of the disease is not tenable, because Rosenberger found them at all stages. How, then, are such discrepancies to be accounted for? All sources of contamination seemed to have been excluded by

<sup>10</sup> *Centralb. f. allg. Path. u. Path. Anat.*, 1908, xix, 934.

Rosenberger in his investigation, but Burnham and Lyons, and more recently Brem, have demonstrated at least one source through which error can arise. Brem,<sup>11</sup> intent upon confirming or refuting Rosenberger's work, and finding acid-fast bacilli fairly constantly, although his inoculation experiment in guinea-pigs proved negative, was led to suspect the water he made use of for his solutions and also his chemicals and stains. All were critically examined for the presence of the acid-fast organisms, but with no result until at last, after fixing the sediment from the distilled water upon a slide by means of albumin, he was able to demonstrate acid-fast organisms in greater or less numbers in every specimen examined. It is true that Rosenberger examined his solutions and also with negative results, but as Brem points out, the failure to find the water bacilli may have been due to the fact that no albuminous material was used as a fixative. Both at Bryn Mawr Hospital and at the Henry Phipps Institute the water used for making the various solutions is distilled from a Jewell apparatus. Inasmuch as of the five positive findings four were from cases in the Bryn Mawr Hospital, some contaminating factor was suspected. The water had already been examined and no acid-fast organisms discovered, for the very reason that may have led Rosengerger into error, namely, the lack of a fixative, for when the sediment from the distilled water at the Bryn Mawr Hospital, where the bacilli had been found, was examined many acid-fast organisms were discovered, and when the water at the Henry Phipps, where practically no bacilli had been found, was examined, no acid-fast organisms were found. In summing up, it seems clear that tubercle bacilli do not constantly circulate in the blood of tuberculous individuals, though they are occasionally present, as is shown by the inoculation experiments of Liebermeister. Being very few in number, they must be extremely difficult to find, otherwise out of 50 cases so carefully studied some should have revealed themselves.

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## IS THROMBO-ANGIITIS OBLITERANS RELATED TO RAYNAUD'S DISEASE AND ERYTHROMELALGIA?

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IN March, 1908, in a preliminary communication, I presented to the New York Pathological Society the results of my studies on the vessels of cases of so-called endarteritis obliterans. At that time I demonstrated that the lesions of endarteritis obliterans of the lower

<sup>11</sup> Jour. Amer. Med. Assoc., 1909, liii, 909.

extremities (or, as the Germans call it, *Spontan-Gangrän*, *Angiosklerotische gangrän*) are not due to proliferation of the intima, but are thrombotic in nature; that, in this disease, there is extensive obliterating thrombosis in the arteries and less often in the veins of the lower extremities, followed by organization and canalization with an attempt at the production of sufficient collateral circulation. I, therefore, suggested that the names *endarteritis obliterans* and *angiosclerotic gangrene* be dropped in this connection, and that the term *thrombo-angiitis obliterans* be employed.

My investigations at that time were particularly aimed at throwing light on the pathology, although I had already collected notes on the symptomatology of more than twenty-five cases. Since then I have dissected and examined twenty additional amputated lower extremities, making twenty-eight<sup>1</sup> in all, and have carefully followed the clinical course of more than fifty patients. In a paper which appeared in this JOURNAL,<sup>2</sup> as well as in two succeeding contributions, one on the condition of the veins,<sup>3</sup> and the other on the symptom complex presented by associated migrating phlebitis of superficial veins,<sup>4</sup> it was definitely stated that a distinct clinical and pathological entity, *thrombo-angiitis obliterans*, was under consideration. In the same issue of this JOURNAL,<sup>5</sup> Sachs, writing on "Raynaud's Disease, Erythromelalgia and the Allied Conditions, and Their Relation to Vascular Disease of the Extremities," expressed views which are completely divergent from my own, with the result that a great deal of confusion has arisen in regard to what thrombo-angiitis obliterans really is, and as to how it is related to Raynaud's disease and erythromelalgia. Having received a number of inquiries on this topic of late, I wish to state my own view briefly here.

Thrombo-angiitis obliterans is in no way related to either Raynaud's disease or erythromelalgia. Patients suffering from thrombo-angiitis obliterans, however, may present a clinical picture which has been and is sometimes diagnosticated as one or the other of the two latter conditions.

The following statement is found in Sachs' paper: "According to Dr. Buerger's studies the morbid changes are the same whether the case be designated clinically as erythromelalgia, Raynaud's disease, or acrocyanosis." This is a rather unfortunate misunderstanding. My own clinical observations lead me to the opinion that the designations erythromelalgia and Raynaud's disease are not applicable to the usual clinical pictures characteristic of thrombo-angiitis obliterans. It is the redness in the dependent position, a striking symptom of thrombo-angiitis obliterans, and the pain that may lead the clini-

<sup>1</sup> These will be reported in detail by the author and Miss Adele Oppenheimer.

<sup>2</sup> AMER. JOUR. MED. SCI., 1905, cxxxvi, 567.

<sup>3</sup> Jour. Amer. Med. Assoc., 1909, pp. 1319 to 1325.

<sup>4</sup> International Clinics, vol. xiii, 19th series, pp. 85 to 106.

<sup>5</sup> AMER. JOUR. MED. SCI., 1905, cxxxvi, 560.

cian to think of erythromelalgia, and the gangrenous termination which may cause confusion with Raynaud's disease. I would digress too far from my theme were I to adduce all the evidence I possess in favor of the assumption that the red blush is but an expression of the attempt to compensate for impoverished circulation by virtue of dilatation of superficial capillaries. It is a phenomenon found also in certain cases of arteriosclerosis or diabetic gangrene, although less striking in these latter conditions.

Some ten years ago Sachs and Wiener, in papers on erythromelalgia,<sup>6</sup> endeavored to show by the pathological findings in a case that the lesion in erythromelalgia is an obliterating process of the arteries. Cassirer, in his monograph<sup>7</sup> on Vasomotor and Trophic Neuroses, expresses the view that they were dealing with a case of "endarteritis obliterans," or, as I term it, "thrombo-angiitis obliterans." This, too, is my conviction.

Of late I have been able to prove by the clinical and anatomical study of two cases<sup>8</sup> that belong to the group of "acrocyanoses,"<sup>9</sup> that gangrene can occur without organic arterial change. This is in all probability also true for Raynaud's disease.

Thrombo-angiitis obliterans is a clinical and pathological entity characterized by thrombotic occlusion of arteries alone or of arteries and veins, giving subjective manifestations, chief among which are pain and the peculiar symptoms of intermittent claudication, and presenting objective phenomena, the most important of which are redness in the dependent position of the limb, marked blanching in the elevated position, evidences of arterial occlusion in the form of pulseless vessels, trophic disturbances of moderate extent and of even grave consequence often terminating in gangrene of one or both lower extremities. We possess no data which tend to show that either erythromelalgia or Raynaud's disease is dependent upon organic obliteration of arteries or veins. Clinically, thrombo-angiitis obliterans may show many variations from a set form, and this accounts for the fact that the true condition is so frequently overlooked. Associated migrating phlebitis and symptoms of intermittent claudication are but two of a number of phases that may stand out as striking features. Individual characteristic symptoms of thrombo-angiitis obliterans do not justify us in establishing a relationship between this disease and others in which somewhat similar phenomena may be found.

<sup>6</sup> Mount Sinai Hospital Reports, 1898, and Phila. Med. Jour., June 29, 1901.

<sup>7</sup> Vasomotorisch-trophischen Neurosen, Berlin, 1901, pp. 145, 163, 164, 193.

<sup>8</sup> To be published with Miss Adele Oppenheimer.

<sup>9</sup> They could be regarded as atypical cases of Raynaud's disease.

## FOUR CASES OF CERVICAL RIB, TWO OF THEM FLAIL-LIKE.

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DEPARTMENT OF HEALTH; VISITING PHYSICIAN TO THE PHILADELPHIA  
GENERAL HOSPITAL, DEPARTMENT OF TUBERCULOSIS.

THREE of the following cases occurred at the State Dispensary for Tuberculosis (No. 21), one in the service of Dr. John C. Da Costa, Jr., one in that of Dr. Samuel A. Munford, and one in my own. The fourth case was kindly added by Dr. John Speese from the Surgical Dispensary of the University Hospital. I am indebted to Dr. Alfred Stengel for the interesting skiagram of a case in which cervical rib was suspected clinically, but which the *x*-rays showed to be the elongated transverse process of the first thoracic vertebra.

It is not my purpose to review the literature of cervical rib nor to discuss the classification, diagnosis, symptoms, or treatment, as this has all been done by others, notably by Keen.<sup>1</sup> The usual types of cervical rib are relatively so frequently discovered today as to be unworthy of detailed report on account of any rarity of the condition or of any special clinical interest pertaining to it. But it seems not out of place to put on record two of the following cases, showing, as they do, a curious and uncommon anomaly, namely, a cervical rib with a distinct joint or articulation in its continuity, being flail-like and having two sections.

So far as I have been able to observe, the diagnosis of cervical rib, certainly in the great majority of instances, and even in the absence of symptoms to call attention to the condition, presents no difficulties (though it should always be confirmed by the *x*-rays). It would be much more frequently detected were careful clinical methods more generally followed in routine dispensary work. This has been particularly suggested by the discovery of the three cases in the State dispensary service within a relatively short time, especially as each of the patients had been previously treated at several other hospitals and belonged to what might be termed the indigent itinerant sick.

CASE I.—L. D. (State Dispensary, Case No. 880, service of Dr. Francine), a white female, aged twenty-nine years; married; a Russian Jewess; five children. There is no family history of tuberculosis and no history of contact with it. The stated illness began two months previously with some blood spitting and cough, a few night sweats, and loss of weight. The highest weight in health was 135 pounds; the present weight is 122 pounds. Height, five feet

two inches. Temperature A.M., 99.2°; pulse, 84; respirations, 20. The pulmonary lesion is an active infiltration of the right apex moderately advanced.

The patient says that for the last two years she has had occasional mild pains in the left shoulder with an occasional "pricking" sensation in the left forearm; she has no pain at present.

*Physical examination* reveals a small mass in the cervical end of the supraclavicular fossa about an inch above the clavicle, which might readily be mistaken for an enlarged gland, except that it is of bony hardness and immovable, and upon deep palpation may be traced back to the cervical spine. There is no general tenderness, but firm pressure upon the mass gives slight pain. Upon the right side a similar and smaller mass may be palpated, with less distinctness. The skin of the shoulders and arms is normal. There is no pulsation or other signs.

Dr. Henry K. Pancoast, the röntgenologist to the Hospital of the University of Pennsylvania, has kindly described the radiogram (Figs. 1 and 2) as follows:

CASE I.—*Right Side.* There is a rudimentary cervical rib about one inch long and tapering to a pointed free extremity. The head is ill-defined and probably not well developed. The neck is obscured by the shadow of the transverse process. There is a very close articulation with the transverse process of the seventh cervical vertebra. A joint line can just barely be determined, and a thickened portion of bone indicates the tubercle of the rib. At a first glance, however, the appearance is almost that of an abnormally developed transverse process rather than of a rib. The *first rib* on this side articulates with the first dorsal body only, and not with the lower edge of the seventh cervical in addition, as is almost always the case when a cervical rib is present.

*Left Side.* The following interpretation of the appearance of the cervical rib on this side is offered after a careful study of the radiogram. There is a poorly defined and not well-developed head articulating with the seventh cervical body. The neck is short and slender. A well-developed tubercle articulates with the transverse process of the seventh cervical vertebra. This articulation is structurally well developed and is clearly defined. The body of the rib appears to be approximately about one and one-half inches long, and terminates in a slightly broadened and distinct articular surface. With the latter a second body seems to articulate. There is a well-defined appearance of a joint. There is sufficient space between the articulating ends to suggest the presence of articular cartilage. This second body is about the same length as the proximal one. The head of the *first rib* on this side seems just barely to touch the lower margin of the seventh cervical body, being a little higher than the head of the first rib on the opposite side.

This unusual radiographic appearance has not previously been



observed by me either in the dozen or more cases examined personally or in radiograms made by others. Neither were any reports of such a type of cervical rib found when making a partial review

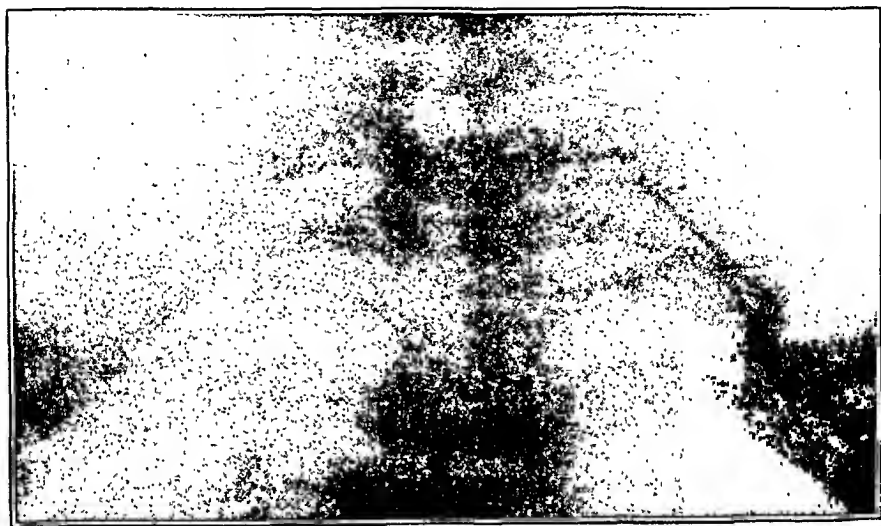


FIG. 1.—Bilateral cervical rib (Case I). Note the flail-like rib on the left, with a distinct articulation or joint in its continuity.

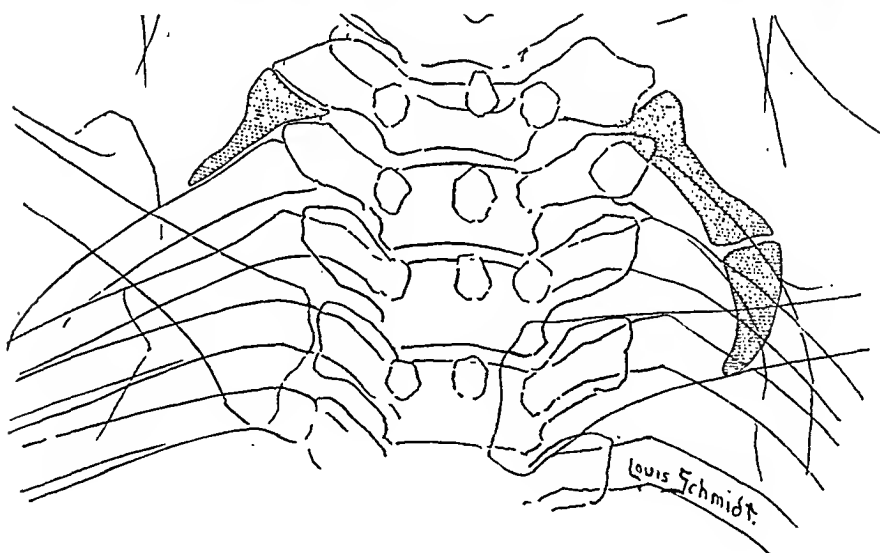


FIG. 2.—Tracing of the skiagram shown in Fig. 1

of the literature on the subject, in 1902. A lack of knowledge concerning more recent literature renders any conception as to the frequency of occurrence of this unusual form impossible.

CASE II.—L. M. (State Dispensary, Case No. 1409, service of Dr. J. C. Da Costa, Jr.), a white male, aged thirty-three years, married; native of the United States. One child. No family history of tuberculosis and no history of contact. The stated illness began four months previously with cough and expectoration, some hoarseness, and loss of weight. Some blood spitting occurred in the last month. The highest weight in health was 158 pounds, the present weight is 136½ pounds. Height, five feet seven and one-half inches. Temperature A.M., 98.4°; pulse, 94; respirations, 24. The pulmonary lesion is an infiltration of the right apex, moderately advanced.

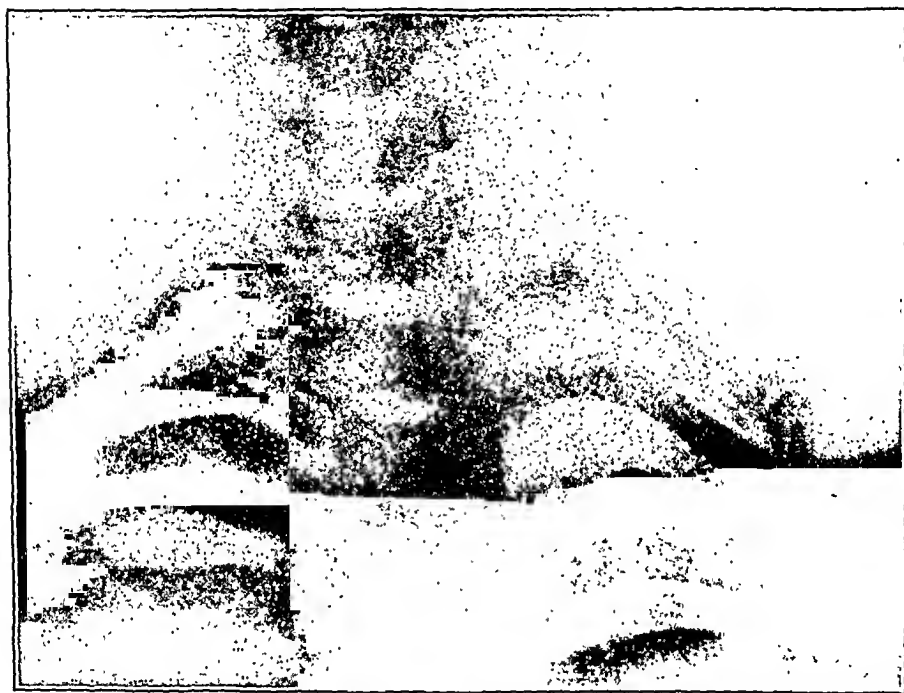


FIG. 3.—Bilateral cervical rib (Case II). Note the flail-like rib on the left, with a distinct articulation or joint in its continuity.

He complains of some pain in the left shoulder; at times this is sharp; no tenderness.

*Physical Examination.* One and a quarter inches above the left clavicle and toward the cervical end of the supraclavicular fossa a small, hard, nodular mass is felt, extending backward toward the cervical spine. Deep palpation in the right supraclavicular fossa reveals a corresponding, though much smaller, nodule. The shoulder and arms are otherwise normal.

The following interpretation of the radiogram (Fig. 3), made by Dr. Menges, of the Jefferson Medical College Hospital, is based upon a comparative study of the radiograms of both cases:

*Right Side.* A complete rib articulating at its origin with the body and transverse process of the seventh cervical vertebra. The

body terminates in front probably in a common cartilage with the first rib, the inner end of which is lower than on the left side, as is usually the case. The *first rib* on this side articulates as it would normally, just as in the first case, with the first dorsal body only, and not with the body of the vertebra above in addition.

*Left Side.* A well-formed but more slender rib. The head is poorly developed, the neck narrow, and the tubercle small, as compared with the same portions of its fellow of the opposite side. At a point corresponding to about the middle of a complete rib, it terminates in a broadened and distinct articular surface. It here articulates apparently with a second bone about one and one-half to one and three-quarters inches in length. The latter tapers to a point, but terminates rather indefinitely, being obscured by the superimposed shadows of the first rib and spine of the scapula. Its termination would seem most likely, however, to be like that of a cervical rib of the third degree in development.

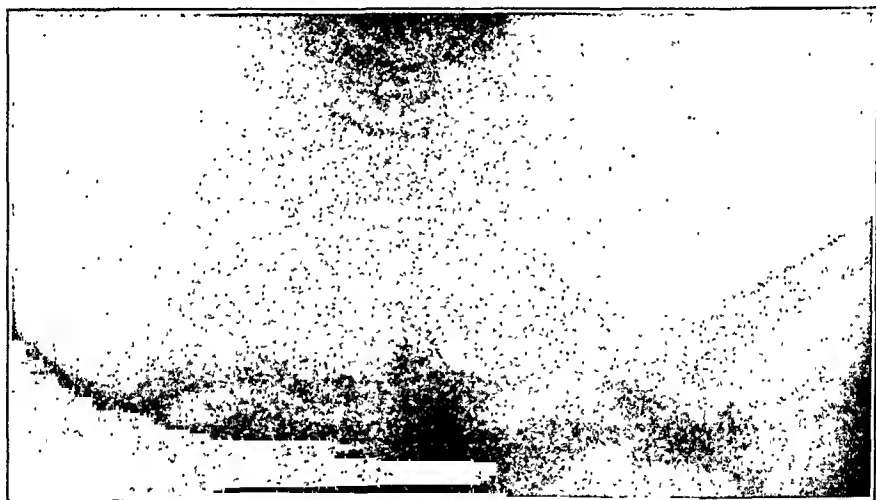


FIG. 4.—Radiogram of a case which clinically suggested a cervical rib. The real condition was an elongated transverse process of the first thoracic vertebra with great obliquity of the first rib. (To be compared with Figs. 1 and 3.)

The *first rib* on this side articulates with the body of the first dorsal and lower margin of the body of the seventh cervical vertebra, as is usually the case when cervical ribs are present. It has a longer neck than its fellow of the opposite side, and the transverse process of the first dorsal vertebra is longer on this side than on the right.

CASE III.—J. T. (State Dispensary, Case No. 1387, service of Dr. S. A. Munford), a white male, aged twenty-five years, presented himself at the State Dispensary for Tuberculosis for an examination as to the condition of his lungs. The past history was not of special importance. The individual was tall and gaunt, with the typical thorax of advanced pulmonary tuberculosis. In

the right superclavicular fossa was a tumor, while the superficial veins from the right arm were distended. Palpation proved the tumor to be somewhat yielding and hard, with a large artery lying upon it. The left fossa contained a somewhat similar tumor distinctly palpable, though not visible. There were no symptoms, nor had there been any. In answer to questions, he stated that his attention had been called to the mass once previously, that being the first intimation of its presence.

The two objects were thought to be cervical ribs, and this diagnosis was confirmed by two skiagrams, one taken by Dr. Menges, and one by Dr. C. L. Leonard. They reveal a double cervical rib, each about three inches long, with well-developed head, neck, and tubercle. Both articulate with the seventh cervical vertebra. The first rib on the right side articulates with the lower margin of the seventh cervical, while the one on the left does not.

CASE IV.—Patient of Dr. John Speese. An unmarried woman, aged twenty-three years, was admitted to the Surgical Dispensary of the University Hospital, complaining of pain, numbness, and tingling of the right arm and forearm. The symptoms began one year previously, and had gradually grown worse, and were accompanied with loss of muscular power and cyanosis of the arm. She was unable to account for this condition, and there was nothing in her past history which was suggestive. Examination of the right arm showed decided weakness of the muscles, but no atrophy. The arm was cold on palpation, and the right radial swollen and weaker than the left, but the two beats were synchronous. The axilla was negative. In the cervical region, directly beneath the sternocleidomastoid and making this muscle rather prominent, a hard mass was palpable. The mass was immovable and felt like a portion of rib. The diagnosis of cervical rib was made, confirmed by *x*-rays, and operation recommended. The patient refused operative interference and did not revisit the dispensary. There were no symptoms produced on the left side. The *x*-rays showed bilateral cervical ribs.

The skiagram was taken by Dr. H. K. Pancoast, who reports as follows:

*Right Side.* An incomplete rib about two and one-half inches long by radiographic measurement, with well-developed head, neck, and tubercle. It articulates with the seventh cervical vertebra. The body is unusually stout, being thicker than the posterior portion of the first rib, and terminates abruptly in a somewhat expanded extremity, presenting an appearance which was at first mistaken for an articular end. The head of the first rib on this side seems barely to touch the lower margin of the body of the seventh cervical vertebra.

*Left Side.* Incomplete rib of about the same length, articulating with the seventh vertebra. The head is not so well developed

as on the other side, and the neck is longer and more slender, corresponding to the greater relative length of the transverse process of this vertebra on this side. The tubercle is likewise not so well developed. The body is more slender and tapers down to a pointed extremity, unlike its fellow. The first rib does not seem to be in relation with the body of the seventh cervical vertebra on this side, its articulation being lower than on the right.

As Cases III and IV conform to the usual type of cervical rib, it was considered unnecessary to reproduce the skiagrams in the text.

Keen, presumably referring to this flail-like condition of a cervical rib, says: "In several cases a joint has been noticed some distance from the first rib, in which case the specimen might be described as a cervical rib articulating with a longer or shorter exostosis. Not uncommonly, this projection from the first rib, which, so to speak, rises up to a greater or less extent to meet the rib, is apt to be thickened at the point of junction and produces a tumor consisting of two portions nearly at right angles to each other."<sup>2</sup>

From a careful study of the skiagrams in Cases I and II herewith reported, I feel that the second portion of the cervical rib is not an exostosis from the first rib, but a true phalanx or distal segment of the cervical rib itself.

I think this is the more likely explanation on theoretical and anatomical grounds, for while the tip of this portion is not distinctly visible in the skiagrams, being merged in the shadow of the first rib and spine of the scapula, yet there is the absence in this position of any dense shadow, as would likely be the case if it were an exostosis and formed a base. The slender, tapering character of this bone, its small end being in juxtaposition with the first rib, and the angle it assumes in relation to the first rib, taking a direction upward and inward, also tend to confirm my view.

<sup>2</sup> See Weissenstein, Ehrich (Madelung), Quervain, Ranzi, Adams, Avon, Tillmanns, and Borchardt.

## REVIEWS.

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EXERCISE IN EDUCATION AND MEDICINE. By R. TAIT MCKENZIE, A.B., M.D., Professor of Physical Education and Director of the Department, University of Pennsylvania. Pp. 406; 346 illustrations. Philadelphia and London: W. B. Saunders Co., 1909.

EXERCISE has for many years been dealt with by authors more or less qualified to write about it from different standpoints. A half-century ago Taylor wrote on the *Movement Cure*, with special reference to the system of Swedish gymnastics. Forty years ago Maelaren's *Physical Education*—although two-thirds of it was a mere description of the use of gymnasium apparatus, and resembled a Spalding catalogue—was greeted as epoch-making. Thirty years ago Blaikie's *How to Get Strong* (in spite of the execrable English of its title) had a considerable vogue. Twenty years ago a translation of Angerstein's *Home Gymnastics for the Sick and the Well*—largely another list of movements and contortions supposed to accomplish remarkable results—was widely consulted. About this time White recorded his opinions under the title, *A Physician's View of Exercise and Athletics*, and many other magazine articles dealing with various aspects of the subject have since been published. Sargent's *Health, Strength, and Power* (1904) was a book of some merit, but was disappointingly elementary and much overloaded with illustrations of special exercises. During this time very valuable treatises on artistic anatomy—the best of which was Arthur Thomson's—and very valueless essays on *The Culture of Beauty* have been published. So far as we know, however, no single book in English has covered this entire field in a manner that is at all comparable with Professor McKenzie's treatise, either for scientific accuracy, literary skill in the presentation of the subject, or comprehensive consideration of all the collateral and allied topics. It has—as the title indicates—two main subdivisions, *Exercise in Education* and *Exercise in Medicine*.

In Part I the author has tried to interest and instruct the individual—layman or physician—who is interested in exercise, whether as to his own habits or in relation to schools and playgrounds, and who, in either case, desires to have some guide in reaching a conclusion. In Part II the application of exercises to pathological conditions is taken up, and, for example, flat-foot, round shoulders,

scoliosis, circulatory and nervous diseases, obesity, locomotor ataxia, and nutritive disorders are dealt with.

There is much to praise and selection is not easy, but some of the more striking features of the book may be noted.

The differentiation of exercises into those of endurance and those of effort is discussed fully, and the overlapping of these classes is clearly defined. For the first time in a book on exercise the physiological condition, as indicated by facial expression, is shown and is illustrated by original masks, confirmed by instantaneous photographs. The physiological chemistry of muscle is set forth and original observations with the Stanton machine on blood pressure are recorded; there is a full discussion of the variations in blood pressure in exercises of effort and endurance; the relation of the nervous system to exercises of skill, strength, and endurance is explained. The effects of elimination are shown by observations on football players at Pennsylvania, and also by tracings from Lombard's balance, published for the first time. There is a new classification of gymnastic apparatus given, and the German and Swedish systems of exercise are described.

The various "systemettes" are summarized. The Japanese "Jiu Jitsu" is illustrated from original sources that have not hitherto been generally available. The article is the most dispassionate and comprehensive review of the merits and demerits of this system that is to be found in English.

One chapter covers the period of growth from infancy to maturity, and contains valuable original classifications of games, exercises, and gymnastic apparatus; it ends with a concise prescription of exercise for sedentary men of middle age. Another gives those facts connected with the construction and management of playgrounds that should be familiar to every physician, teacher, or member of any city or town council who wishes to know accurately how playgrounds should be established, equipped, or conducted. It is illustrated by plans and photographs of playgrounds in operation. The exact amount and the nature of the exercises that should form part of the day's course for school children, from the kindergarten to the high school, including school-yard games, are set forth in a clear and interesting manner.

There is a short historical sketch of physical education in the early American colleges, with a full description of the department of physical education at Pennsylvania, and with illustrations of the forms used, of classes at work indoors and outdoors, and an outline of a typical year's course. This is followed by a discussion of the ideal physique of the college student, illustrated by Dr. McKenzie's statuette, the "Athlete," and by a complete set of original photographs of classes at work.

The physical education of the blind and deaf-mute is for the first time carefully described.

The treatment of mental defectives in schools and institutions—showing the best exercises and the possibilities for improvement in different grades—is summarized in an original and practical way, and for the first time. This concludes Part I, which has thus covered the physical education of the normal and the slightly defective individual from infancy to maturity, and has dealt with various minor subjects.

Part II opens with a general chapter on the application of exercise to pathological conditions, describing, for example, the use of massage in sprains, the place of exercise in the treatment of pulmonary tuberculosis, and the value of deep breathing in the prevention and cure of disease. Original drawings and photographs of the anatomy of the foot, and of its mechanics, are given in connection with the treatment of flat-foot. Round-back, stoop-shoulders, and scoliosis are discussed, and the movements and musculature of the spine and thorax are described in this connection most completely and thoroughly. Numerous tracings taken from Dr. McKenzie's cases illustrate the various forms of curves. The treatment by exercise and the prognosis in functional and in osseous curves are judiciously discussed. Typical prescriptions for the three most common forms of curvature are given, and are illustrated by original photographs and reports of cases.

The whole question of exercise and athletics as a factor in the production of disorders of the circulation is reviewed, the general conclusion being that athletes are slightly longer-lived than non-athletic students. The relation of athletics to arteriosclerosis remains undetermined, but there does not seem to be any definite evidence that they hasten its onset. Oertel's treatment and the Schott treatment are fully considered, and there are original illustrations of each movement, and of the movements suggested by Satterthwaite. The role of exercise in cases of obesity (in addition to diet, and the use of thyroid extract) is covered, and there are well illustrated prescriptions of exercises and an outline of the way in which they should be modified. Gout, diabetes, and rheumatism are also discussed in a general but very satisfactory manner. The treatment of constipation by massage, by vibration, and by duplicate and active movements is thoroughly described. The section on hernia is new and somewhat radical, but is most interesting. The final chapter is devoted to the treatment of the nervous system. This has not been so fully considered in any book on exercise that we have seen.

The book as a whole is not only the most thorough and satisfactory yet written on the subject, but it is the most modern and scientific. It may readily be understood by the layman, yet is replete with information valuable to the professional man, but not usually in his possession. It is, moreover, interesting throughout, and can be read for pleasure as well as for profit.

J. W. W.



THE PROBLEM OF AGE, GROWTH, AND DEATH. By CHARLES S. MINOT, Professor of Comparative Anatomy, Harvard Medical School. Pp. 280; 73 illustrations. New York and London: G. P. Putnam's Sons, 1908.

IN this book Dr. Minot has collected the views which from time to time he has expressed in various papers and addresses, upon the subjects included in the title, the volume being cast in the form of a series of public lectures delivered before the Lowell Institute and illustrated by reproductions of lantern slides used at the time of presentation.

After outlining the characteristics of senility the author points out that the structural evidences of senescence of cells consist in the assumption of structural and physiological differentiation, in cytomorphosis; that with a few exceptions this consists, from a morphological standpoint, in the decrease in nuclear material in the cells and in the growth of the protoplasm; and that the evidence of the youth of cells is the converse of these characters, the increased proportion of nuclear matter and the small amount of protoplasm. With this basis and with the realization that with differentiation cells lose their power of active multiplication possessed as an eminent character in their youth, he points out that senescence, the process of differentiation and maturing, finds its greatest rate of development in the earliest periods of existence of the complex organism, highest in the earliest embryonic periods, and rapidly lost through later embryonic life to the extent that the rate of growth at the time of birth is but a small percentage of what it was in the early proliferations occurring at this period, and in postnatal life quickly descends to an almost level minimum in earliest childhood. This rate of growth he estimates by weight comparisons, and correlates it with evidence of cell proliferation (mitotic index) in the tissues, recognizing that body growth is the result rather of cell multiplication than of increase of cellular size. In other words, paradoxical though it seem, we grow old most rapidly in the antenatal and earliest postnatal life, and progressively less and less rapidly as temporal age advances. Rejuvenescence, manifested in a limited sense in regenerative processes and repair of waste in nature, finds its highest and most satisfactory manifestations after sexual fertilization of the female germ cell in the inception of the fresh generation; and the utility problem narrows down to that of slowing cellular senescence after maturation and before actual senility (for senility in the stages of cytomorphosis is not only a progressive differentiation, but in addition degeneration which is followed by death of the cell and its removal). This problem has no immediate answer, but to the mind of the author is not unpromising of some solution. This phase of the matter receives less consideration than one might hope, although the author undoubtedly escapes much that may be rash in prognosti-

cation. It surely must lie, at least in part, in attempting to adjust the organism so as to escape the omnipresent but adventitious causes of wear and tear from excess of function, of infection, and of accident. Whether with such influences eliminated there be a possibility of further slowing the rate of senescence into actual senility and to natural death is the more precise point which the author believes is perhaps possible, but which he acknowledges as at present unanswerable in satisfactory manner. The fact that thermic and chemical conditions have been shown to influence cellular growth, multiplication, and differentiation affords reason for suspecting that there may be in the future some return to the inquiry.

Natural death does not follow in the same train in the complex and the simple monocellular organism. In the former at the time of birth the vast bulk of the component cells are free from changes necessitating their demise, they die because of the loss of some important group whose existence and functional ability are essential to the harmonious life of the whole body group. In the monocellular organism, however, natural death depends upon the wearing out of the single cell. The author doubts (and it would seem very properly in the light of the numerous examples which within the past decade have been established of sexual reproduction following an asexual cycle in protozoa) whether the older idea of the essential continuity of matter and virtual immortality of monocellular organisms should be accepted. They probably follow the same lines as seen in higher organisms, rejuvenescence by conjugation or definite sexual fertilization, senescence progressing through a series of asexually reproduced organisms until the later members of the cycle are so deteriorated that they become unviable or are restored by a second fertilization. So in this sense is there a continuity of the germ plasm of the higher organisms, through an isolated group of germ cells developing into the sexual cells with the differentiable body cells developing in each generation from this continuous stem.

The author does not in the general text advert to the real nature of life; but is entirely frank in that in one of his appendices (page 272) he deliberately states his belief that no theory of life so well harmonizes with its recognized manifestations as one which includes the existence of a mysterious and as yet untouched vital force working through the multimorphic and multikinetic protoplasm as a physical basis.

The book is well adapted for the laity as well as for scientific readers, its simplicity of style and the many presentations of the personality of the author in familiar relation giving it no little charm. The matter is not so much the presentation of new as the novel presentation of that which has been known, but not applied in quite the manner and for the purpose of the present author. That the rate of growth is greatest in the earliest periods has long been appreciated; Cohnheim, for instance, used this fact as a sustaining argu-

ment for the verity of his theory of tumor formation, claiming that thus tumors, which spring from "cell residua," representing early embryonic periods, must grow much more rapidly than those coming from rests developing later. Richness in nuclear matter, small proportion of protoplasm, absence or incompeteness of differentiation have long been regarded as evidence of the youthful type of cells and the converse of mature cells. But the particular adaptation to show that age progresses most rapidly in the earliest, and more slowly in the more advanced periods of life, is new and of interest and significance. It has its more immediate bearing upon the broad biological conception of life and living things, but may well find eventual application, even though at present from the utilitarian standpoint it seems no more than collateral evidence of the reasonableness of efforts to prolong life to a natural death at a later period than is ordinarily seen in human beings. It would be no matter of advantage to intelligent beings that differentiation should be slowed in the period of extreme youth, even could such a result be effected; the senescence of differentiation of structure and function must be accepted for the acquirement of that grade of intelligence and other functions which make life worth the living, even though the price of the acquisition be inevitable death. In the slowing of the post maturation stage rests the real problem, not necessarily involving the entire mass of component cells of the system, but at least those groups essential to bodily persistence and performance of functions essential to the individual. Whatever the answer, it cannot evade death; rejuvenescence of the individual is impossible, it can merely look to the prolongation of the mature period of life; much aging must necessarily have already been experienced, and it can only lie (adventitious causes of disease and death being disregarded) in more perfect maintenance of functional harmony in the body, in the avoidance of partial and general functional excesses and (what is in reality the same thing) in adjusting by will or by environment the rate of living to the simplest needs.

A. J. S.

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PROTOZOÖLOGY. By CARY N. CALKINS, Professor of Protozoölogy in Columbia University, New York. Pp. 349; 125 illustrations; 4 colored plates. New York and Philadelphia: Lea & Febiger, 1909.

WHATEVER the ultimate quantitative limit of the field of protozoölogy in medicine, there can be no doubt that it must be accorded the qualitative dignity of bacteriology as a branch of study dealing with the causation of disease. That it should at present be less developed than bacteriology, of course, can easily be under-

stood when we realize that the cultural methods employed in the latter subject are only in the most limited measure applicable to the protozoa. Moreover, it is doubtful whether we will ever be able to systematize as satisfactory methods for the extracorporeal cultivation of these organisms, owing to the fact that the life history of each is made up of stages more or less distinct from one another and that the conditions for each, in some measure, vary. Further, there is reason for us to believe that even where cultivation is possible, cultural variations of such marked type are likely to arise that it will only be after extensive study that one can establish the identity of the organism in each of such variations. For these reasons protozoölogy must necessarily, to a much greater degree than bacteriology, depend upon morphological studies. This must mean that the investigator must acquire familiarity with a wide range of minute organisms, and each in a number of different appearances; and further, that investigations must, to a very great extent, depend upon the most painstaking microscopic examination of each part of the material under investigation. Time and long preliminary preparation must be demanded of the protozoölogist, and it can scarcely be expected that the ordinary practitioner of medicine will ever be in a position to devote himself, save in a very superficial manner, to such a study. It is possible that such methods of cultivation as have been accomplished by Novy in the case of trypanosomes, or of Musgrave in the case of the amœbæ, may be extended to facilitate the work; but little can be hoped to obviate the very much greater amount of direct individual attention to morphological characteristics of the material on the part of the trained laboratory worker than is required in bacteriology.

Dr. Calkins' book is an evidence of the growing interest which the medical profession holds toward the protozoa, and the fact that it is written by a protozoölogist rather than by a medical man indicates the difficulties which would be encountered by the latter in the study of these intricate life histories. While Dr. Calkins inveighs against the restriction of protozoölogy to pathogenic forms, and urges upon the profession the very great value of the study of the protozoa in the appreciation of the various vital processes, both normal and pathological, yet the reader will not be disappointed in his expectation of finding that the work deals largely with the pathogenic forms.

The book is based upon a series of lectures before the Lowell Institute in 1907. The first portion (which closely recalls the author's former book on *The Protozoa*) is devoted to a systematic discussion of the general organization of protozoa, their physiological activities, and the phenomena of their life cycle, a separate chapter being given up to conjugation, maturation, and fertilization. An extremely important chapter is devoted to parasitic relations of the protozoa, the lives of these organisms as parasites, the modes

of transmission, the exogenous life of protozoan parasites, and reference to the effects of protozoan parasites upon their hosts. The latter chapters of the book are given over to consideration of pathogenic varieties. Under the flagellates, the spirochetes and their position in nature are fully discussed; and various problems that have arisen in connection with the amœba and dysentery, the nigri bodies in rabies, Guarnieri's bodies and smallpox, as well as obscure diseases subject to protozoan origin, are fully discussed.

Dr. Calkins' reputation as a protozoölogist and the close and much appreciated interest which he has taken in medical problems in which protozoölogy has application are a guaranty of sympathetic and full consideration of such questions. The work undoubtedly is a forerunner of other books upon the same subject, and will itself be the basis of studies in our medical laboratories in protozoölogy. It is admirably adapted as a text-book in schools where it is contemplated this branch may be taken up as part of the course of instruction; and while it does not pretend to include all forms of known pathogenic protozoa, and therefore cannot be regarded as a systematic treatise, it is an absolutely essential volume in the laboratory of every worker in clinical or general pathology or in any branch of etiology.

A. J. S.

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THE PRINCIPLES AND PRACTICE OF PHYSICAL DIAGNOSIS. By JOHN C. DA COSTA, JR., M.D., Associate in Clinical Medicine in the Jefferson Medical College; Chief of the Medical Clinic and Assistant Visiting Physician to the Jefferson Hospital, Philadelphia. Pp. 548; 212 illustrations. Philadelphia and London: W. B. Saunders Company, 1908.

DR. DA COSTA has prepared a very excellent work on physical diagnosis, of which forty-five pages are devoted to the general methods, four hundred to the thorax, and sixty-four to the abdomen. The book is distinctly readable. The descriptions are, as a rule, clear, sufficiently detailed, and written evidently by one who possesses not merely a book knowledge of the subject, but who has tested for himself and reached definite conclusions upon the majority of the methods that he describes. Each section is introduced with a brief paragraph upon the clinical anatomy, and each disease described is preceded by a paragraph upon the clinical pathology. The latter paragraphs constitute a valuable addition to the book, and at any rate for the student, serve to make more understandable the physical signs that are subsequently described.

It is not to be supposed, however, that Dr. Da Costa is greatly superior to his predecessors in overcoming some of the inherent diffi-

culties of the subject. His discussion of the quality of percussion sounds is practically a statement that sounds have different qualities. In his discussion of pitch, he regards the sound elicited by percussion apparently as a single note and not, as it really is, a complex of vibrations of different rates.

The section on the examination of the thorax is enriched with many satisfactory illustrations that, without repetition, serve to emphasize the points brought forth in the text. As in other works of this character, the nude human female serves as a model upon which to sketch the various outlines and symbols that are supposed to elucidate the description of the physical signs. This seems to us an unnecessary subordination of science to assumed art. Aside from this the diagrams and illustrations and, in particular, the sphygmocardiograms are of unusual excellence. The signs to which proper names are attached are given quite fully, but it would be of advantage if references to the original article or work were appended. Dr. Da Costa has evidently preferred not to quote literature, although he is undoubtedly familiar with it, and in this manner has probably lessened the bulk of his book, but even for students, we think, some references are desirable.

There are a few points to which we should like to call attention. He fails to mention the fact that a normal percussion resonance may occasionally be obtained over a pneumothorax cavity. The diagrams of the respiratory and cardiac sounds add little if anything to the description from the text. It should be noted that *cegophony* may be heard over as well as above a pleural effusion. The paragraph on the physical signs of bronchiectasis is inadequate, and is misleading in so far that the dilatation of the small bronchi, which is the commonest pathological condition of this nature, does not give rise at any time to the signs of cavity. In regard to the movable dulness of the pleural effusion, it is stated that it is rarely demonstrable as a result of change in posture of the patient. This is surely not the common experience. Kussmaul's *pulsus paradoxus* has not in our experience been frequently demonstrated in obliterative pericarditis, and Friedreich's diastolic collapse of the jugulars is an equally elusive sign. Dr. Da Costa is one of the few writers who calls attention to the enfeeblement of the second sound at the base as significant of myocarditis. He speaks too confidently of the existence of relative pulmonary regurgitation.

The section on the examination of the abdomen and the abdominal viscera is entirely inadequate. The illustration of enteroptosis is rather an exaggerated than a usual form of this condition. The description of the examination of the intestines is very brief and auscultation is dismissed with a disparaging paragraph.

Much could be said in praise of the different parts of this book were it not for the restricted space at our disposal.

J. S.

**TUBERCULOSIS: A PREVENTABLE AND CURABLE DISEASE.** By S. ADOLPHUS KNOFF, M.D., Professor of Phthisiotherapy in the New York Post-graduate Medical School and Hospital. Pp. 394; 115 illustrations. New York: Moffat, Yard & Co., 1909.

THIS book, dedicated alike "to the Masters of Medicine, to the Noble Men and Women, and to the Statesmen and Philanthropists who strive for the eradication of the Great White Plague," can be appreciated by those in all walks of life. To the consumptive himself it is offered, not to replace the services of the physician, but to show him how to live. To all, the author trusts that the volume may lend assistance.

Clearly and comprehensively the book stands out as one of the best which has appeared upon the subject. Chapters I, II, and III are devoted to the duties of the patient, people, and physician, respectively. In chapter IV suggestions are made so that the patient may receive sanatorium treatment at home. The remaining chapters point out the duties of employers, school teachers, the clergy, charity organizations, etc. A brief description of the various state sanatoria is included. Emphasis is laid upon the value of the "preventorium" as well as the sanatorium. Municipal measures, which have been instituted for the establishment of out-of-door schools, day camps, dispensaries, etc. are described. No phase of the subject is omitted. Numerous photographs lend attractiveness to the book and these are well described in the text. The author not only graphically describes the subject in hand, but many suggestions of betterment are made, among these being the solicitation of the government in providing adequate disinfection of mail bags. The book forcibly reflects the great enthusiasm of its author. Though the diction is generally simple and appreciable to the lay mind, now and again "scientific digressions" occur—pardonable, in view of his enthusiasm. Attractiveness of style and thoroughness of compilation are features.

W. T. C.

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**THE HISTORY OF THE STUDY OF MEDICINE IN THE BRITISH ISLES.** By NORMAN MOORE, M.D. (Cantab.), Fellow of the Royal College of Physicians, Physician to St. Bartholomew's Hospital, London. Oxford: At the Clarendon Press, 1908.

THESE four lectures are very fascinating for one who is interested in the history of the development of medical science. The author evidences a vast store of erudition upon which he draws, and he presents it in such an attractive manner that the reader is carried along with interest and pleasure. The first lecture treats especially of Dr. John Mirfeld, in whose person was exemplified what old Cotton Mather termed "the angelical conjunction of physic and

divinity." Along with his account of this fourteenth century physician, Dr. Moore offers us a brilliant picture of the state of medical knowledge and the conditions of medical study in the England of that period. The second lecture describes the education of physicians in the seventeenth century in London, dealing especially with that of Edward Browne. The author shows how in this century dissection and observation supplanted the reading and studying of the ancients, which had constituted the education of physicians during the previous centuries. In the latter part of the seventeenth century, dating from the period of the Restoration in England, men of intellect turned with vigor to the study of natural phenomena. As J. R. Green says, they were wearied with the subtleties of religious disputation, and the reaction against Puritanism extended not only into their moral life, but led to an intellectual reaction which was fully as important, if not more so. It was at this time that the Royal Society was founded. We are all familiar with the galaxy of distinguished names including those of Newton, Locke, Boyle, and Flamsteed, in addition to the eminent physicians, Sir Theodore Mayerne, Harvey, and Sydenham, who were among its earliest and most famous members. Of course, it is to the members of the medical profession that Dr. Moore directs particular attention, but the passion for medical research which arose at this time can only be correctly studied as a part of the great scientific spirit which then permeated the nation. In the third lecture Dr. Moore gives us a number of interesting clinical notes made by Sir Theodore Mayerne on various patients of high rank, including James I, Charles I and his Queen. He also tells us of the work of Mayerne, Sydenham, and Glisson, and shows that it was by their practice and writings that the study of clinical medicine was established in Great Britain. In the fourth lecture he continues his subject down into the eighteenth century, and then gives a most interesting digression on the early history of medicine in Ireland and Scotland. We know of few lecturers who have condensed as much really valuable material into so small a space and, at the same time, have been able to tell their story in such an interesting manner. F. R. P.

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A MANUAL OF OTOTOLOGY. By GORHAM BACON, A.B., M.D., Professor of Otology in the College of Physicians and Surgeons, Columbia University, New York, with an introductory chapter by CLARENCE JOHN BLAKE, M.D., Professor of Otology in Harvard University. Fifth edition; pp. 508; 147 illustrations and 12 plates. New York and Philadelphia: Lea & Febiger, 1909.

WITH each edition Bacon's *Otology* is not only increased in size, but, if possible, improved in its arrangement and contents. The book has long since been recognized as the representative American



manual of otology. To the present edition Dr. Bacon has added a number of new illustrations and a concise but excellent account of the operation of tonsillectomy and the submucous resection of the nasal septum. This edition, like each of the previous editions, shows every evidence of careful revision of the text on the part of the author. Every subject is brought thoroughly up to date. No better book could be recommended to the student or practitioner who wishes an authoritative presentation of the subject of otology. F. R. P.

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ILLUSTRATIONS OF THE GROSS MORBID ANATOMY OF THE BRAIN IN THE INSANE. A SELECTION OF SEVENTY-FIVE PLATES SHOWING THE PATHOLOGICAL CONDITIONS FOUND IN POSTMORTEM EXAMINATIONS OF THE BRAIN IN MENTAL DISEASE. By I. W. BLACKBURN, M.D., Pathologist to the Government Hospital for the Insane, Washington, D. C.; Professor of Morbid Anatomy in the Medical Department of the University of Georgetown, and in the Department of Medicine of the George Washington University, Washington, D. C. Pp 154; 75 plates. Washington: Government Printing Office, 1908.

OUR knowledge of the gross morbid anatomy of the brain in the insane is by no means as complete as it should be, and Dr. Blackburn has done a real service in presenting this work, in which there are 75 excellent plates. The technical difficulties in preparing the photographs for such a work as this are many, and the author is to be congratulated for the excellent results obtained. No one who has not worked in neuropathology can appreciate the many difficulties which beset the preparation of brains for such a work as this, and it is indeed a pleasure to commend the good results obtained.

The collection of pathological specimens from which the photographs were made were selected from among 2350 autopsies, and the author has endeavored to give examples of most of the common changes in the adult insane. He has followed a pathological classification rather than a clinical one, and the specimens include brains from general arteriosclerosis with or without cerebral softening, hemorrhages, atrophy of the brain, meningo-encephalitis or paresis, hydrocephalic states, meningeal conditions, and brain tumors. As the author states, it is of course understood that the lesions represented in no sense are to be considered as showing the essential morbid anatomy of any form of mental disease except general paralysis and possibly senile dementia and arteriosclerotic dementia. In many instances the lesions were purely accidental and had nothing to do with the form of insanity. Opposite each plate is a brief statement of the name, age, and clinical diagnosis, with a more extended, but brief, discussion of the lesions. T. H. W.

# PROGRESS OF MEDICAL SCIENCE.

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## MEDICINE.

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UNDER THE CHARGE OF

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**Acute Addison's Disease.**—STRAUB (*Deut. Arch. f. klin. Med.*, 1909, xcvii, 67) reports a case of Addison's disease, which is of importance as throwing light on the time relation between the onset of the pathological process in the adrenals and the beginning of clinical symptoms. This is the most acute case yet reported, the duration of the disease being only seventeen days. The onset was marked by severe abdominal pain and vomiting. There was, at times, watery diarrhoea. Ten days later reddish discoloration of the skin appeared over various points of pressure. These later assumed a more brown color. There was no pigmentation of the mucous membranes. The blood pressure remained 105 mm. Hg., until the day of the death, when it fell to 99 mm. The clinical diagnosis was malignant tumor of the lungs, pyloric stenosis, and tumor in the right lumbar region. The symptoms, pigmentation, asthenia, psychical disturbance, and sudden death also suggested Addison's disease. Autopsy showed scirrhus carcinoma of the pylorus with multiple metastases. Both adrenal glands were involved, but only to a very moderate degree. The most striking lesion of the adrenals was a general venous thrombosis, the apparent age of which corresponded well with the duration of the symptoms. Straub believes that the obstruction to venous outflow was the etiological factor in the case.

[There are a number of cases in literature in which destructive processes in the suprarenal capsules have resulted fatally, and in a considerably shorter period of time with symptoms closely similar to those described in this case. Indeed, a syndrome consisting particularly of sudden abdominal pain, vomiting, diarrhoea, tachycardia, asthenia, psychical disturbances, hypothermia, collapse, often similar to that

observed in peritonitis, and sudden death, has been described by Sergent and Bernard (*Compt. rend. soc. de biol.*, Paris, 1898, 24 see.; *L'insuffisance surrénale*, Par., Masson, 1903, Collection Léauté), as characteristic of acute insufficiency of the adrenals. In the works referred to a number of interesting illustrative cases may be found. The striking feature in this case appears to be the rapid appearance of the pigmentation which, however, does not seem to have been especially characteristic.—W. S. T.]

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**Two New Tests for Albumin in the Urine.**—OGURO (*Zeit. f. exp. Path. u. Therap.*, 1909, vii, 349) presents two new qualitative tests for albumin in the urine. Were it not for the fact that his tests are apparently specific as well as simple, he would hesitate to add to the already long list. Test I, with tincture of iodine and sodium bisulphate. Method of application: A few cubic centimeters (5 to 6) of the urine—which must, of course, be clear—is placed in a test-tube and acidified with a few drops of dilute acetic acid. About  $\frac{1}{2}$  volume of tincture of iodine (10 per cent.) is now added, and the whole is well shaken. A dirty, dark brown precipitate results. A saturated solution (watery) of sodium bisulphate is next added drop by drop, shaking constantly, until the brownish fluid is decolorized. If the urine contains albumin, one sees a permanent whitish cloud or flocculent precipitate. If no albumin is present, the fluid remains clear after the addition of the sodium bisulphate, and shows only the original urinary color. With minimal quantities of albumin, the reaction becomes more evident on standing a few minutes. Test II, with decolorized tincture of iodine. Method of application: One decolorizes tincture of iodine with saturated watery solution of sodium bisulphate and filters. The filtrate is a clear, rather yellow fluid, which keeps well. On standing for some time, small, yellow crystals may be precipitated, without injury to the reagent. The urine, as in Test I, is acidified with dilute acetic acid. About  $\frac{1}{3}$  volume of the reagent is added and the whole well shaken. If albumin is present, a cloud or a flocculent white precipitate forms. With traces of albumin the reaction may be delayed a few minutes. Normal urine never shows a cloud with these tests. For control Oguro has always employed the Heller-Spiegler heat, and the sulphosalicylic acid tests. In two years Oguro has never found a urine in which salts, alkaloids, or other non-albuminous substances led to confusion. The tests are sensitive to albumin in a dilution of 1 to 120,000.

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**Abdominal Palpatory Albuminuria.**—SCHREIBER (*Deut. Archiv f. klin. Med.*, 1909, xcix, 1) has made an elaborate study of albuminuria resulting from certain manipulations in abdominal palpation, in which the aorta both above and below the renal arteries has been compressed and the effect of pressure on the vena cava has been noted. He finds, by the aid of measurements from bony landmarks and of skiagrams, that the renal vessels may be localized with great precision. Spontaneous albuminuria from abdominal palpation is very seldom seen. It certainly is not due to compression of the vena cava, but may easily arise from compression of certain parts of the aorta. Compres-

sion of the aorta at the point where the renal arterics are given off is easily accomplished in suitable cases and always leads to albuminuria. It is seldom the case that one can palpate the aorta above the origin of the renal arteries, but when possible, pressure here also causes albuminuria. In either case the albuminuria is more marked and persistent the more complete the compression and the longer it is maintained. Even an incomplete arterial compression of a few seconds may suffice to produce albuminuria. Arterial albuminurias appear quickly from slight changes in the aortic pressure and are generally of high albumin content. Pressure exerted on the aorta below the renal arteries causes no change in the urine. Compression of the vena cava above the renal veins leads to the development of albuminuria much more slowly, and the albumin appears in relatively small amount.

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**The Staining of Moist Preparations with Azure-eosin (Giemsa).—**GIEMSA (*Deut. med. Woch.*, 1909, xxxv, 1751) has contributed a new staining method which should prove of special interest to those interested in tropical medicine. It is intended for the staining of moist smears and fresh tissue by means of his azure-eosin mixture, which gives the characteristic Romanowsky staining. The details of the method are as follows: (1) Fix the smears while still moist or the tissue in sublimate alcohol. (Concentrated watery  $HgCl_2$ , 2 parts; absolute alcohol, 1 part.) The cover glass is placed in the solution before it dries, with the specimen side down; later it is turned over. Fixation requires twelve to fourteen hours. (2) Wash quickly in water and then five to ten minutes in a solution of KI, 2 gm.; Lugol's solution, 3 c.c.; and distilled water, 100 c.c. (3) Wash in water very quickly and place in a 0.5 per cent. aqueous solution of sodium thiosulphate, by which the yellow staining of the iodine solution is completely removed. (4) Place in flowing water five minutes. (5) Stain with freshly prepared Giemsa solution one to twelve hours. After the first half hour the stain should be renewed. (6) Wash in water and carry through the following: (a) Acetone, 95 c.c.; xylol 5 c.c.; (b) acetone, 70 c.c.; xylol, 30 c.c.; (c) acetone, 30 c.c.; xylol, 70 c.c.; (d) xylol, pure. (7) Embed in cedar oil. The time in solutions (a), (b), and (c) depends on the differentiation desired. The method is especially valuable in the study of protozoa, such as malaria, infusoria, trypanosomes spirochetes, etc. Beautiful results are also obtained with tissue.

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**A Muscle Bundle Between the Superior Vena Cava and the His Bundle.—**THOREL (*Münch. med. Woch.*, 1909, lvi, 2159) reports findings which will be of considerable importance in the physiology and pathology of the heart. By making serial sections and reconstructing a model, he has demonstrated, in two adult human hearts studied, that there is a continuous bundle of muscle connecting the superior vena cava with both the Keith-Flack nucleus and the Asehoff-Tawara nucleus. This bundle is readily distinguishable histologically, consisting of Purkinje cells. A detailed account will appear soon.

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**The Excretion of Uric Acid Injected Intramuscularly in Gouty Subjects.—**Brugsch and Schittenhelm have given uric acid and purin bases to

gouty patients with purin-free food and have studied the elimination of uric acid in the urine and feces. As there was always the possibility of bacterial decomposition in the intestines, BENCZUR (*Zeit. f. exp. Path. u. Therap.*, 1909, vii, 339), at the suggestion of Brugsch, injected a known quantity of uric acid intramuscularly to determine how much of it could be recovered. As the procedure is not without unpleasant consequences, such as marked local and constitutional symptoms, Benczur omitted controls on normal individuals, obtaining them from the literature. The work of others has shown that healthy persons excrete 50 to 99 per cent. of uric acid injected intramuscularly. Benczur repeated the experiment on a patient suffering with gout. He injected 0.5 gm. uric acid into the gluteal region; the patient had been on a purin-free diet for several days, and it was found that the average daily output of endogenous uric acid was 0.2101 gm. During the two days immediately following the injection 81.6 per cent. of that given had been excreted. Benczur believes it not unlikely that the increase was due in part to the destruction of leukocytes, because of the marked local reaction, together with fever and general malaise, which followed the reaction. The same occurred in the normal individuals reported in literature. The experiment shows that the gouty patient eliminated uric acid injected intramuscularly just as a healthy subject does. In other words, the renal excretion of uric acid in the gouty is apparently normal.

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**The Effect of Compression of the Superior Mesenteric Artery upon the Systemic Blood Pressure.**—Arteriosclerosis of the splanchnic arteries, presumably on account of its action in setting up increased peripheral resistance to the flow of blood, and thus raising the systemic blood pressure, has long been accounted a cause of cardiac hypertrophy. LONGCOPE and McCLINTOCK (*Univ. Penna. Med. Bull.*, 1909, xxii, 226) have studied this condition experimentally in dogs by noting the changes in blood pressure produced by compression of the superior mesenteric artery. In five minutes the vessel was compressed or ligated forty-three times, and in every instance a rise of blood pressure resulted. The average elevation of pressure varied from 4.5 mm. to 10.3 mm. The changes in arterial pressure seemed to vary in direct proportion to the amount of constriction. When the compression was of short duration the elevation of blood pressure continued until the experiments were stopped, but when the vessel was ligated for a longer period, the primary rise in pressure was, except in one instance, followed by a secondary fall to normal. Compression of the aorta at the level of the diaphragm produced a marked and rapid rise in blood pressure, but neither compression at the bifurcation nor ligation of one or both renal arteries resulted in any alteration in systemic pressure.

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**A Quantitative Index to Tuberculin Treatment.**—The two factors of value in tuberculin treatment are toxin tolerance and reaction. Toxin tolerance is the object to be gained in acute cases which have become afebrile, and it is obtained by the use of doses small enough to avoid reactions. In chronic cases, and in certain others, which, after long

treatment, have come to a standstill, the productions of mild reactions are apparently beneficial. One difficulty in the therapeutic administration of tuberculin has hitherto been the impossibility of determining accurately the dosage, which in a given individual will, on the one hand, give the greatest stimulation without reaction, or, on the other hand, will produce a reaction of mild grade. Basing their work on experience with the cutaneous tuberculin test, WHITE, GRAHAM, and VON NORMAN (*Jour. Med. Research*, 1909, xxi, 225) have formulated a procedure to govern accurate dosage. They have found that a definite ratio exists between the amount of tuberculin applied cutaneously and that given subcutaneously for the production of local and constitutional reactions. Thus, one-fifteenth of the amount of O. T., which when applied to the skin produced the minimal cutaneous reaction (a local redness about 4 mm. in diameter) would, when given subcutaneously produce both local and constitutional reactions. One-thirtieth of the same amount subcutaneously would produce local without constitutional reaction, while one-fiftieth produces neither local nor constitutional reaction. Thus, by the use of a definite quantity of O. T. on the skin, it is possible to determine (1) the borderland of reaction and absence of reaction to tuberculin which will be the degree of tolerance to tuberculin of the patient, and (2) the dose of tuberculin necessary to give the grade of reaction desired. In their cutaneous tests, the authors used 0.01 c.c. of various percentages of O. T., and protected the point of application with a vaccine shield in order to allow complete absorption.

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**The Treatment of Pneumonia by Leukocytic Extract.**—Continuing the work of HISS, FLOYD and LUCAS (*Jour. Med. Research*, 1909, xxi, 223) have used extracts of leukocytes in the treatment of 41 cases of pneumonia. The leukocytes were obtained from the exudate produced by the injection of aleuronat into the pleural cavities of rabbits. While the general mortality of lobar pneumonia is given by Musser as 21 per cent., the mortality of this series was only 12.2 per cent. Of the 5 fatal cases, 2 were bronchopneumonia in children, 2 were complicated by cardiac lesions, and 1 was a man, aged seventy years. About 44 per cent. terminated on or before the sixth day of the disease. The most striking result of the treatment was a definite constitutional improvement, relief of labored respiration, and improvement of such symptoms as might be due to toxemia. The extract was administered subcutaneously in doses of 10 c.c. twice daily. In no instance did the treatment do any harm, but in three instances an urticarial eruption appeared after an interval of four to seven days. Following the beginning of inoculation there was a steady diminution in the number of leukocytes in the peripheral circulation. The evidence of effect on the process in the lungs was not distinct.

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**Aseptic Purulent Meningeal Exudates.**—WIDAL (*Revue mens. de méd. interne et de thér.*, 1909, i, 1) has considered carefully that group of cases showing the signs of meningitis in which lumbar puncture gives a thick, purulent but sterile exudate. An exudate of this character was first described as occurring in syphilis, but has since been met with in la grippe, pneumonia, puerperal eclampsia, uremia, suppurative

otitis, after spinal cocainization, in mumps, and in meningeal conditions of unknown origin. The process may be a slow latent one, or it may begin with acute, alarming symptoms. On bacteriological examination of the spinal fluid, cultures, staining, and inoculations all prove it to be sterile. Especial stress is placed on the histology of the polynuclear cells present, for Widal asserts that the fact that these cells retain their normal structure is in itself evidence of the sterility of the fluid. For examination the sediment of the centrifugalized fluid is fixed on a slide and stained with hematin and eosin. In septic exudates the contour of the cells is indistinct, and both nucleus and protoplasm undergo marked changes. In sterile exudates the nucleus has a delicate texture, the protoplasm is perfectly homogeneous with fine granules, and the contour of the cell is distinct. The great importance of recognizing cases of meningitis with sterile exudate is that, in spite of what may appear to be a most unfavorable condition, the prognosis is excellent, for most cases result in complete recovery.

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**Experimental Transmission of Acute Poliomyelitis.**—FLEXNER and LEWIS (*Jour. Amer. Med. Assoc.*, 1909, liii, 1639) have issued a preliminary report of their experiments in the inoculation of monkeys with the material obtained from two cases dying of acute poliomyelitis. An emulsion in salt solution of the spinal cord from the children, and later emulsions of the spinal cord of previously inoculated monkeys, were introduced through a trephine opening in the skull. In each instance the inoculated animal became paralyzed after a somewhat variable period. Histological study of the spinal cords of the monkeys showed in every case lesions similar to those of poliomyelitis in man. [It is difficult to overestimate the importance of this communication. The power of reproducing the disease in an indefinite series of animals may well prove to be the first step in the production of a curative or preventive serum.—W. S. T.]

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**Arteriosclerosis of the Pulmonary Artery.**—While the lesser circulation is usually unaffected in cases of generalized arteriosclerosis, in certain cardiac conditions, and especially in mitral stenosis, the pulmonary vessels alone may show signs of degeneration. LANBRY and PARVU (*Tribune méd.*, 1909, xlii, 484) report the case of a girl, aged twenty years, who had never had any rheumatism or any other infectious disease, but who had suffered with cardiac symptoms for many years. The diagnosis of mitral stenosis was made, and was confirmed at autopsy when the mitral opening was found to be nearly occluded. The aorta and the smaller arteries of the general circulation were in a practically normal condition, but the pulmonary arteries showed thickening and sclerosis in their whole extent. Lanbry and Parvu agree with Vaquez and Giroux, who have reported a similar case, in believing that the underlying cause in the production of this localized arteriosclerosis is the hypertension resulting from the narrowing of the mitral orifices. They also consider that the frequent and profuse pulmonary hemorrhages which occurred in their patient were greatly facilitated by the diseased condition of the vessels.

## S U R G E R Y.

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UNDER THE CHARGE OF

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**Rupture of the Biceps of the Arm.**—LEDDERHOSE (*Deut. Zeit. f. Chir.*, 1909, cl, 126) says that according to his observations, neither a pure traumatic rupture of the biceps nor a traumatic separation of the upper pole occurs. The dislocation of the outer belly outward, which has frequently been described and illustrated, occurs in most cases spontaneously. The position of the long head of the biceps and the resulting defect are caused by arthritis deformans of the shoulder-joint. It is an occupation deformity. In the overwhelming number of cases described in the literature as traumatic ruptures of the biceps, there already existed pathological changes in the biceps tendon, and the trauma acted as the exciting cause. The occurrence of an indirect, purely traumatic rupture of a biceps tendon, not already invaded by a diseased process, must be doubtful. The very widely accepted view that an indirect, traumatic rupture occurs generally at the upper juncture of muscle and tendon, is not well supported. It appears questionable whether an indirect, traumatic rupture occurs in this portion. A rupture of the distal tendinous portion of the biceps at its insertion into the radius or in the immediate neighborhood appears to be determined by a preceding pathological process. Wounds of various grades in the muscular portion from direct trauma, have been repeatedly observed. Whether tears of the muscle substance can occur from indirect trauma has not been shown satisfactorily by the literature of the subject. The conditions which have been described as herniæ of the biceps, are, almost without exception, cases of dislocation of the outer belly of the biceps.

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**The Surgery of the Heart.**—SALOMONI (*Archiv. gén. de chir.*, 1909, iv, 881) had previously collected and reported 134 cases of cardiorrhaphy. He now calls attention to some new facts concerning this operation. He approaches the heart through the intercostal space which is the seat of the external opening of the wound, enlarging the wound by scissors and disarticulating from the sternum one or two adjacent costal cartilages. For wounds of the base of the heart or of the right cavity he advises a transverse section of the sternum. By retraction, an opening 8 cm. wide can be obtained with this method. He counsels drainage of the pericardium after every cardiorrhaphy, when one is not sure of his asepsis. The reason for it is the same as for peritoneal drainage. The



serosa of the pericardium absorbs less than that of the peritoneum, and intrapericardial collections of blood are absorbed slowly. Of 58 cures, in 30 pericardial drainage had been practised. Pericardial effusion is frequent after cardiorrhaphy. It localizes itself posteriorly to the heart, and produces precordial oppression, anxiety, and weakness. The frequency of the pulse and cyanosis of the face appear only late. Up to the present time Salomoni has collected 158 cases of cardiorrhaphy. Of these, 59, or 37.33 per cent., were cured, and 99 died; 21 died before the end of the operation or soon after. There were 2 cases of double wound of the heart, and 1 case of gun-shot wound with the missile remaining in the ventricle. Some cases are irremediably mortal from simultaneous lesions of both cavities, valvular lesions, or lesions of the motor centres. Wounds of the heart through and through are not always fatal. In 5 such cases the posterior wound was unrecognized. Lesions of the coronary arteries are often fatal from arrest of the heart, cardiac degeneration, infarct, and aneurysm. Ligation of one of the branches of a coronary artery can be followed by a cure. The branches of the coronary arteries are not terminal, so that their successful ligation is possible. If the heart is arrested during cardiorrhaphy, light massage can make the heart beat anew. For the diagnosis of a cardiac wound, one should take into account, the seat of the wound, the symptoms of internal hemorrhage, increase of the cardiac dulness, the appearance of oppression, precordial distress, cyanosis, and rapidity of the pulse.

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**A Comparative Study of the Value of Internal Urethrotomy and of Divulsion.**—CIMINO (*Ann. d. mal. d. org. gén.-urin.*, 1909, ii, 1361) says that the supporters of each of these two operations defend their positions forcibly up to the present time. He studied the subject from the standpoints (1) of the lesions and histological changes produced from the time of the operations to the final results, and (2) the septic phenomena, local and general, occurring after each operation. As the work was done on animals, traumatic strictures alone were studied. He traumatized the urethras, on the same day and by the same method, of ten animals, of the same species, of the same weight, and with urethras of the same calibers. Although the work was done only on traumatic strictures, Cimino believes that the results can be legitimately applied to the gonorrhœal type. Internal urethrotomy produces, at the site of the stricture, a linear, longitudinal, and regular section, the depth of which is preëstablished. As the wound widens it is transformed into a triangular or rectangular space opening into the urethra. It cicatrizes on the surface with a thin layer of fibrous tissue under the epithelium. The lesion produced by urethrotomy is strictly localized, so that it affects the stricture tissue only at the line of section. Divulsion produces tears of variable importance, and may pass in all directions. Upon healing, these lesions produce numerous extensive and irregular cicatrices, which reproduce the original lesions. New deformed and capricious strictures are added to the original one. The general aspect of the divulsed urethra varies according to the time when one observes it, but it is always characteristic. Immediately after the operation it presents as a bursted hollow organ; 8 days later it appears as a torn and fringed canal. When the lesions have become definite, the urethra appears as a rigid pipe, or a canal the surface of which is re-

duced to shreds. Divulsion terminates in the total transformation of the stricture into a cicatricial ring, with some epithelial elements scattered in the homogeneous, compact, fibrous tissue. These are always found on the surface of the urethra and in the glandular cavities, but they present the phenomena of proliferation and degeneration. Internal urethrotomy is, therefore, superior to divulsion. The septic condition of the urethra does not exercise any influence upon the choice of one or the other of these operations, as neither guarantees against the development of infectious lesions, local or general.

**The Operative Treatment of Ununited Fractures.**—CREITE (*Deut. Zeit. f. Chir.*, 1909, cl, 267) reports observations on 30 cases of ununited fracture operated on in Braun's clinic. The most frequent cause of non-union (18 cases) was the interposition of soft tissues between the fragments. The tibia was involved in 28 cases, the femur in 1 and the humerus in 1. In 17 cases the fracture was simple and in 13 compound. The time of operation was from four to twenty-eight weeks after the accident. In most cases (18) Bier's passive hyperemia and percussion at the seat of fracture, had been tried for several weeks, without success. In 15 cases, the old Dieffenbach method was employed, the seat of fracture being freely exposed by a flap incision. Ivory pegs were introduced, one above and the other below, into holes drilled through the bone, and the pegs were cut off level with the surface of the bone. In some cases, one of the bones of the leg was fixed with the ivory peg, and the other with wire sutures. The course of the healing was undisturbed in all, the pegs healing in. In no case was it necessary to remove the pegs secondarily. The time necessary for union varied from five weeks to twenty-eight weeks, the average being eight and one-half weeks. In one case, in which a steel nail had been employed, union failed. In 14 cases the ends of the fragments were resected and sutured together. One of these died eleven days after the operation from sepsis. In this case, however, there had been a compound fracture of the leg, and there had been an acute osteomyelitis of the tibia for about fourteen years. Three and a half weeks after his admission to the clinic, the necrotic bone was removed and the ends of the bone sutured. In 2 cases no bony union took place. In one there had occurred a severe compound fracture, with a torn, soiled wound, followed by severe suppuration and destruction of the periosteum of the fragments. The wire suture led to the formation of a fistula, and later the suture was removed. In the second case there had been a compound fracture of the humerus, with the loss of a 7 cm. piece of the whole thickness of the bone. The remaining 11 cases left the clinic with union, but in some the healing had been troublesome, and in 4 cases the suture had to be removed later on account of fistulæ. As a result of these experiences the Dieffenbach method is given the preference over the resection method.

**Resection of the Middle Portion of the Duodenum.**—KAUSCH (*Zent. f. Chir.*, 1909, xxxvi, 1350) says that resection of the descending portion of the duodenum may become desirable for various causes. A frequent and probably the most important indication seems to be a carcinoma of the papilla of Vater. The operation most frequently done is by a

transduodenal or retroduodenal approach. After it is determined that the case is not one of gallstones, the tumor with the neighboring portion of the duodenum is excised, and provision made for the proper evacuation of the common bile duct and pancreatic duct. Körte's case lived three and three-quarters years after operation. Those of Halsted and William J. Mayo were both soon followed by recurrence. Kausch thinks this is one of the most favorable of cancers for removal, because it becomes recognizable early and when yet small, owing to the severe jaundice without colic which it causes, and which drives the patient to the surgeon for relief. It then lies in the wall of the duodenum, remains localized a long time, and does not metastasize until late. This portion of the intestine is easily removed, but the anastomosis of the gall and pancreatic ducts complicate the operation considerably. No severe operation should be done in the presence of severe jaundice. The gall and pancreatic ducts should not be introduced at the line of sutures in the divided bowel, as that would give an untrustworthy anastomosis. The operation should be performed in two stages. In the first, Kausch, upon opening the duodenum, found a bean-sized nodule exactly at the papilla of Vater, with no metastasis, no gallstones but the gall-bladder about the size of the fist. An anterior cholecyst-enterostomy was performed with a small Murphy button, about 50 cm. from the plica duodenojejunalis, and about 12 cm. lower an entero-anastomosis with a large Murphy button. Ten days after the operation the large, and three days later the small, button passed the rectum. The jaundice disappeared and the weight improved slightly. Sixty-seven days later the second operation was performed. Numerous adhesions lengthened the first part of the operation. The anastomoses made in the first operation were in good condition. The duodenum was isolated up to the pylorus, the head of the pancreas separated from it, and a posterior gastro-enterostomy was performed. The pyloric end of the stomach was closed blindly; the duodenum beginning above was shelled out, taking away with it a piece of the head of the pancreas the size of a walnut; the bile duct was ligated; the duct of the pancreas was cut open in the pancreatic tissue; and the duodenum divided somewhat above the junction of the descending and inferior portion. The remaining lower open end of the duodenum was sutured, hood-like, over the cut surface of the pancreas with catgut sutures. This area was covered over with omentum, a cigarette drain introduced, and the abdominal wound sutured. Twenty-one days after the operation the patient was well and had increased 2.5 kilograms in weight.

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**The Conservative Treatment of Severe Wounds of the Extremities Threatening Gangrene.**—NOESSEKE (*Zentralbl. f. Chir.*, 1909, xxxvi, 1377) says that in severe wounds of the fingers, especially those from incised and contused wounds, we are often in doubt whether the remaining narrow and poorly nourished bridge of skin will permit the hanging part to live. The conservative treatment frequently fails. The cause of the gangrene is the deficient arterial supply and the retarded outflow of venous blood. The venous stasis is the most prominent symptom in these wounds, as in cases of frost-bite. High elevation with moist warm applications are usually employed to overcome the circulatory disturbances, and frequently fail. In several severe finger wounds,

in a case of frost-bite of both thumbs, and in a case with asphyxia threatening gangrene from Raynaud's disease, a broad incision was made to the bone anteriorly, beginning below the level of the nail and extending over the end of the finger. The success was astonishing. The wound was tamponed with gauze soaked with camphor oil to prevent adhesion of the wound surfaces. The hand, including the wounded finger, was then exposed by a suction apparatus to a negative pressure of about 12 to 15 cm. of mercury for eight to ten minutes. This was kept up for a week, and applied two or three times daily. In the beginning there escaped dark cyanotic blood, drop by drop. Later arterial blood welled forth, which daily increased in amount. This passive hyperemia treatment had been tried repeatedly in the case of Raynaud's disease, and had failed completely. The incision was, therefore, the chief cause of success. In the cases so treated the sensation returned in a few hours, and the wounded part lived and retained good function. Further observations must determine how valuable this method will prove to be in the involvement of larger portions of the limbs. It may prove of value in threatening or advancing gangrene of other origin, plastic operations, transplantation of organs, and for the improvement of the circulation through the sutured vessels.

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**The Role of Heart Massage in Surgery.**—WHITE (*Surg., Gynec., and Obstet.*, 1909, ix, 388) says that heart massage is an established method of resuscitation, ten successful cases having been reported by ten operators. Heart failure is rarely primary in chloroform anesthesia. It is, therefore, essential that respiration be invoked by artificial means in conjunction with heart massage. Artificial respiration alone will not inaugurate heart contractions nor maintain blood pressure. The best results have been obtained by the subdiaphragmatic method. The most frequent indication for its use is chloroform narcosis with cessation of respiration and circulation. In other conditions of heart failure secondary to respiratory failure, and not dependent upon organic changes in the heart, the method is applicable. Further use of the method will widen its field of usefulness. The possibility of resuscitation bears a definite relation to the time that has elapsed between the cessation of the heart beat and massage. The briefer the interval the more rapid is the response to heart massage. White says that the entire question is unsettled, that the 50 cases tabulated is only an incentive to further research, that each additional case is of value, and that some time may yet elapse before we can adjust heart massage in proper accord with its surgical bearings.

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**Bone Sarcoma.**—BUERGER (*Surg., Gynec., and Obstet.*, 1909, ix, 431) adduces the following facts from a careful study of twenty bone sarcomas: To the expansive type belong the phenomena of "ping-pong" or "egg-shell" crackle. Bone expansion is a feature of a majority of the bone sarcomas examined, and occurs in the shaft as well as in the extremities of the long bones. We should recognize the diffuse infiltrative variety as one which may remain latent until pathological fracture occurs; and should remember that normal bone contour is not compatible with the presence of intramedullary growths. Certain destructive types, causing fusiform enlargement of the part, and very frequently

involving the upper end of the fibula, are malignant tumors that soon penetrate into the soft parts. A combination of chronic osteoperiostitis with central sarcoma may occur. Calcification in the osteoid and chondroid tumors is a feature which may be of great value in diagnosis. Periosteal bone production is also to be utilized in diagnosis. Skiagrams are of great importance in the recognition of these tumors. We should look for the characteristic periosteal bone deposition and especially for dense shadows in the diaphysis as well as in the epiphysis, with a view to diagnosing the sclerosing type of osteoid and chondroid sarcoma. The extensive calcification and the slow endosteal progress exhibited by certain types suggests that early diagnosis may be possible. To discover the presence of endosteal lesions before the more malignant extra-osteal masses have been developed should be a desideratum. Fine, radiographic bone detail is essential for an adequate interpretation of the pathological changes. A large tumor in the soft parts is no reliable measure of the extent of the bone destruction or the size of a central focus if such there be. Large tumors outside of the bone may be associated with a very slight lesion in the bone.

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## THERAPEUTICS.

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UNDER THE CHARGE OF

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**The Use of Atropine Sulphate and Atropine Methylbromide in Diabetes Mellitus.**—RUDISCH (*Med. Record*, 1909, xxvi, 1093) has treated a number of cases of diabetes mellitus with the above salts of atropine. A carbohydrate-free diet was also given at the beginning of the treatment in conjunction with the atropine. His results were so satisfactory that he advises the use of these salts by other investigators. Rudisch sums up the action of atropine in this series as follows: (1) A reduction in the amount of sugar excreted; (2) an increase in carbohydrate tolerance. Under the first heading he says that it was uniformly observed that the glycosuria disappeared much more rapidly under this combined form of treatment than with the customary antidiabetic treatment alone. He calls attention to the fact that while a strict carbohydrate-free diet will usually cause a marked diminution in sugar excretion, traces of sugar will still remain in the urine or appear from time to time. In these cases Rudisch found that the use of atropine in sufficient dosage invariably resulted in a complete suppression of the glycosuria. Interruption in the administration of the drug without change in the diet was followed in many of the cases by the reappearance of sugar in the urine. This glycosuria could always be made to disappear again by resuming the atropine. Rudisch believes that the influence of atropine in increasing

carbohydrate tolerance is manifested in two ways. He found that patients could tolerate much larger quantities of carbohydrates when atropine was administered. He also noticed that the tolerance for carbohydrates increased after the prolonged administration of atropine. He administered the atropine in the form of the methyl bromide and the sulphate. The former has the advantage of being much less toxic, but its effects are not so prompt as those of the sulphate. Its cost, moreover, limits its use. Rudisch advises that methyl bromide should be given to adults in the dosage of  $\frac{2}{15}$  grain three times a day, gradually increasing this by  $\frac{1}{15}$  grain until  $\frac{8}{15}$  grain three times a day are being taken. In one case 3 grains were given daily over a short period with no other toxic effect than dryness of the throat. The initial dose of atropine sulphate should be  $\frac{1}{150}$  grain three times a day, and that may be gradually increased to  $\frac{1}{30}$  grain three times a day. Children require a dosage proportionate to their age. Rudisch observed no toxic effects from this dosage. When a marked dryness of the throat occurred the atropine was discontinued temporarily, or more often the dosage was not increased. No deleterious effect upon the general health was observed from the prolonged administration of these salts of atropine.

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**The Process of Cellulose and Hemicellulose Digestion in Man, and Their Food Value.**—LOHRISCH (*Zeit. f. exper. Path. und Therap.*, 1909, v, 478), in an exhaustive article, concludes a number of previous observations concerning the digestion of the celluloses and hemicelluloses in man. He refutes the prevalent opinion that the cellulose group and the closely allied hemicelluloses are digested in the human intestine by bacterial fermentation. He cites much experimental evidence to support his view that the digestion of the celluloses and hemicelluloses occurs in the same way in man as that of the starches. Lohrisch's conclusions are as follows: (1) Cellulose and the hemicelluloses are closely related chemically. Certain individual chemical characteristics, however, serve to differentiate them. (2) They show no marked differences in their physiological behavior. (3) Man is able to digest 50 per cent. of cellulose and the hemicelluloses under normal conditions. Individuals with habitual constipation are able to digest from 70 to 80 per cent. (4) Man is able to digest larger quantities of the hemicelluloses than of cellulose. (5) The digestion of the hemicelluloses and cellulose occurs in the same way in man as the digestion of the starches; that is, they are converted in the intestines to their corresponding sugar. Their conversion and absorption, however, occur more slowly than is the case with the starches. The quantity absorbed is completely burned up in the human body. Consequently, proteid and fat are saved from katabolism. Probably glycogen is also stored up in the tissues if an excess has been absorbed. Cellulose and the hemicelluloses are not split up into the volatile fatty acids in the small intestine. Probably only a small portion of the unabsorbed material is changed in the large intestine to the volatile fatty acids, and as such, re-absorbed. (6) Cellulose and the hemicelluloses are harmless substitutes for the ordinary easily absorbable carbohydrates. The hemicelluloses are of practical worth as substitutes when ordinary carbohydrates are not well borne.

**The Influence of Different Carbohydrates upon the Glycosuria in Diabetes.**—WERBITZKI (*Zeit. f. exper. Path. und Ther.*, 1909, vi, 235) has tested in several diabetics the effect of different carbohydrates upon the excretion of sugar. He gave his patients a meat and fat diet for from three to five days in order to determine the grade of glycosuria on a non-carbohydrate diet. He then tried the effect of different carbohydrates upon the excretion of sugar, separating the carbohydrate periods by meat and fat periods. He used for this purpose bread, rice, buckwheat, milk, potatoes and oatmeal. Of these substances oatmeal by far seemed best adapted to supply the necessary carbohydrates for diabetics. The authors conclusions are as follows: (1) The different carbohydrate-containing substances exercise an entirely different influence upon the glycosuria of diabetics when these substances contain the carbohydrate in pure form; (2) oatmeal in large quantities causes in many cases of diabetes no increase in the glycosuria, therefore oatmeal has a special place among the carbohydrate containing foods; (3) this action seems to be specific in the case of oatmeal and possibly may be explained by a peculiar difference in the chemical composition of oatmeal compared to the other carbohydrates; (4) the oatmeal diet exercises in the majority of cases a favorable effect upon the glycosuria. At the same time the general condition improves and the subjective symptoms become less marked. Therefore, oatmeal is to be preferred to the other carbohydrate-containing substances in the treatment of diabetes; (5) finally, in order to secure the best results from the use of an oatmeal diet, Werbitzki believes that it is necessary to exclude all other carbohydrates from the diet.

**The Treatment of Gastric Ulcer.**—MAYERLE (*Arch. f. Verdauungskrank.*, 1909, xv, 337) reviews the various methods for the treatment of gastric ulcer, and reports his results in 71 cases treated by the Lenhartz method. His cases include 29 recent, bleeding gastric ulcers, 17 chronic, and 25 uncomplicated, acute cases; 65 per cent. were cured in a short time. A slower recovery without recurrence was noted in 11 per cent. of the cases, and with recurrence in 14 per cent. No benefit was obtained in 10 per cent. of the cases. There were a few cases in which the diet was not tolerated. Mayerle could detect no injurious effects, even when the diet was commenced immediately after the hemorrhage. He found that the Lenhartz diet occasionally seemed to increase the tendency to hyperchlorhydria. In these cases he advises an increase in the proportion of fat in the diet and, at the same time, a reduction in the proportion of albumin. In the chronic cases with reduced acidity, a diet with less albumin, a moderate amount of fat, and an increase in the carbohydrates seemed to give the best results.

**Optic Atrophy from the Use of Atoxyl and Arsacetin.**—PADERSTEIN (*Berl. klin. Woch.*, 1909, xxii, 1023) describes in detail a case of optic atrophy occurring as a result of injections of atoxyl. He also discusses 6 similar cases reported by different observers. Besides these cases with well-defined optic atrophy, Paderstein was able to find in the literature reports of 22 cases of severe disturbances of sight from the use of atoxyl. He could determine no relation between the size of the dose used and the severity of the disturbance of the sight. In the

typical cases the injury is manifest by a concentric diminution of the field of vision beginning on the nasal side; which finally leads to a diminution of central vision and often to complete blindness. The harmful effect of atoxyl extends to the nerve elements of the retina and consequently disturbances of color vision especially violet blindness, may be caused. Less often a narrowing of the retinal arteries is noted. Paderstein thinks that the poisonous action of atoxyl upon the visual apparatus is probably due to the aniline component. This may be true, since similar results are observed in aniline poisoning, but not in arsenical poisoning. He also says that it has not been actually determined that arsacetin is less dangerous than atoxyl, although this has often been assumed.

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**The Use of Phosphorus in Rachitis.**—SCHABAD (*Zeit. f. klin. Med.*, 1909, lxxviii, 94) reports the results of further studies of the effects of phosphorus on the metabolism in rachitis. In a previous paper he demonstrated that phosphorus, dissolved in cod-liver oil markedly increased the retention of calcium in rachitis. His present paper deals with the effect of the administration of cod-liver oil alone. His experiments showed that it increased the calcium retention but considerably less than when given with phosphorus. He also found that inorganic calcium, when given with phosphorus dissolved in cod-liver oil, was retained to a large extent, and the author, therefore, recommends these three remedies for the treatment of rachitis.

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**The Treatment of Obesity.**—LAISSUS (*Jour. des Prac.*, 1909, xviii, 281), after a study of 200 cases of obesity, recommends as of primary importance a reduction in the amount of carbohydrates and fats ingested. If the patients complain of hunger during the first few days of treatment he allows them to eat fairly large quantities of fresh fruits and green vegetables. He advises frequent small meals with a minimum of salt, to lessen the appetite. Fluids should be restricted at meal times to one-half pint. Since the obese require a considerable amount of fluid, it should be given in the form of drinks one hour before, and three hours after meals. Laissus also advocates the various physical methods such as exercise, hydrotherapy, and massage. Exercise should not be excessive and taken regularly under specific directions. Hydrotherapy is given in the form of hot baths in running water, and the alternating hot and cold shower. Massage, to be beneficial, should be prolonged for some time, and the kneading process is preferable. He believes that drugs are of little use and that thyroidin is actually dangerous. He has found that some cases of obesity are benefited by the administration of a few drops of tincture of iodine in milk. Obesity associated with arteriosclerosis is often beneficially influenced by small doses of sodium iodide.



## PEDIATRICS.

UNDER THE CHARGE OF

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**Hemorrhagic Disease in the Newborn with Direct Transfusion.**—The case reported by SWAIN, JACKSON, and MURPHY (*Boston Med. and Surg. Jour.*, 1909, clxi, 407) was that of an apparently normal newborn baby, whose paternal grandfather had died of pernicious anemia and one of its cousins of melæna neonatorum on the fourth day of life. The baby had nursed normally and had a good meconium movement before going to sleep. It woke up with a sharp cry, and the nurse found its clothes and bed saturated with a bloody stool, there being about 10 ounces of fluid blood. This was repeated several times, the blood being slightly thicker than normal blood. Fresh rabbit serum and diphtheria antitoxin did not check the bleeding, to the bloody stools being added bloody vomiting and hemorrhagic spots beneath the skin. The child was in extremis when direct transfusion from the father's radial artery to the child's internal saphenous vein was employed. The flow of blood was permitted to continue for five to six minutes, terminating in complete cessation of the hemorrhage. The child recovered perfectly. No cause can be given by the author, but the defect was probably not in the vessel walls, as is usually stated, but rather in the failure of the blood producing mechanism, which was remedied by some part of the normal blood which was introduced into the circulation.

**Furunculosis and Acute Pemphigus Neonatorum.**—REICHE (*Deut. med. Woch.*, May, 1909), in the staphylococcal skin infections of children, uses hot packs to promote free perspiration, thereby bringing the cocci near the skin surface, and then uses mercury baths to disinfect the skin. He tried this treatment with much success in furunculosis and pemphigus.

**Glandular Fever.**—J. E. BURNS (*Archiv. Int. Med.*, 1909, iv, 118) reports an epidemic of glandular fever (6 cases) occurring in the Children's Ward of the Union Protestant Infirmary, at Baltimore. The patients were from two and one-half to five years of age. He also reports 3 cases occurring in the family of one of the discharged patients, one arising within twenty-four hours of the child's reaching home. The Children's Ward had been isolated for two months before the appearance of the glandular fever, because of measles, scarlet fever, and diphtheria in Baltimore. In the case of the family infections referred to, the child had not been seen by any of its relatives for two and one-half months. All of the patients had a leukocytosis varying from 18,800 to 26,400, the small mononuclears being chiefly increased. The throats and tonsils of all the patients were injected, but showed

no exudate; the cultures showed *Staphylococcus aureus*. The cervical glands were enlarged on both sides simultaneously in 8 cases; in one case but one side suffered. The swelling and tenderness reached its maximum on the third day. The upper glands were especially affected. All the glands were hard and discrete; none suppurated. Stiffness of the neck disappeared with the tenderness. The portal of entrance was probably the tonsils and pharynx, the etiological organism *Staphylococcus aureus*. Nephritis was not noted in any case.

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**Fœtal Rickets.**—J. R. CHARLES (*Brit. Jour. Children's Dis.*, 1909, vi, No. 67) reports a case of fœtal rickets and discusses the etiology. There was no history of diseased thyroid, tubercle, or syphilis in the family. The child was born with an enlarged head and with deformed bones, which were enlarged at the ends. She did not walk until three years old and the anterior fontanelle did not close until nearly the fourth year. About the fourth year examination showed the following condition: The head was square with marked frontal and parietal eminence; the teeth were badly shaped and carious; there was marked enlargement of the thyroid, both sides and isthmus. The radius and ulna on both sides were slightly bowed out, and the lower epiphyses were much enlarged. There was slight lateral curvature of the spine; and enlargement of the epiphyses of the lower ends of the femora and of the tibiae and fibulae. Both tibiae were much bowed outward and forward. There was distinct beading of all the ribs at the costochondral junction; marked laxity of ligaments and fascia, marked flatfoot, and enlargement of the liver, below the edge of the ribs. The mental condition was bright.

Concerning the etiology of fœtal rickets Charles offers the suggestion that perversion of skeletal growth in intra-uterine life may be due to perversion of the thyroid function, since arrested conditions of skeletal growth are due to an arrested thyroid function, and removal of the thyroid in young animals arrests skeletal growth (Mackenzie). The beneficial effects of phosphorus in rickets may be exerted through the thyroid, since excretion of phosphorus is increased after administering thyroid gland and also in exophthalmic goitre. The good effects of phosphorus therapy in rickets, some claim, is due to improvement in calcium circulation, and the tetany of rickets is attributed to the poverty of calcium in the central nervous system. The thyroid is frequently enlarged during pregnancy, and Blair Bell states he found the blood calcium index low, in cases of hyperthyroidism, as in exophthalmic goitre. Therefore, Charles thinks that possibly the thyroid enlargement in this case is connected with the bony changes and that it is not present as an independent entity.

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**Glioma of the Spinal Cord.**—GEORGE PEACOCKE (*Brit. Jour. Children's Dis.*, 1909, vi) reports the occurrence of glioma of the cord in a girl, aged eleven years, who had suffered no illness except typhoid fever in infancy. Five weeks before her death she suddenly complained of pain and stiffness in her neck, her head being bent over to the left side. This condition continued for one month, her general health remaining as usual. At the beginning of the fifth week she lost power to use her right hand. Malaise developed, and within the next few days severe

pain in the back of the neck and spine, and she could not bear to be moved. There was retention of urine, her right arm became paralyzed, and her right leg could be moved but slightly. Her temperature was at all times subnormal. On admission to the hospital at the end of the fifth week, the slightest movement caused her severe pain. Her face showed a marked cyanotic hue. Respirations were rapid, and a pneumonic area was found in the middle lobe of right lung. Paralysis of right arm and leg developed; sensation was present, both tactile and painful. Paralysis of the left arm and leg developed in a few hours, and death occurred from respiratory failure. Consciousness was retained throughout.

At autopsy there was found apparently a blood clot in the centre of the cord. On cross-section the blood discoloration was found to extend from the level of the thalamus scriptorum downward a distance of 11 cm. into the upper part of the cervical cord. Above, it lay posteriorly to the right side, and below terminated close to the central commissure in the postinternal column of the left side. Microscopic sections from the medulla and upper part of cord showed the structure to be glioma with small diffused hemorrhages. The outer portion was a network of neuroglia-cell processes, small, round cells, and blood-vessels, and inside this a zone of free blood. The small tumor lay in the postero-internal column of the cord, pressing on and distorting the normal portions of the white and gray matter. The crossed pyramidal tract in the right side was degenerated. Points of interest are: (1) The locality of tumor. Tumors of the spinal cord are relatively rare. The ratio to tumors of the brain is 1 to 13. (2) The age of the patient and the character of the tumor. Meningeal intradural spinal cord tumors preponderate over the medullary type, and of the latter tubercle is the commonest cause. (3) The duration of symptoms. This is usually about sixteen months.

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## OBSTETRICS.

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**The Treatment of Retention of Pieces of Placenta with the Occurrence of Fever.**—VEIT (*Zentralbl. f. Gyn.*, 1909, No. 32) describes a case in which fever and hemorrhage continued after labor, and ceased when a piece of placenta was removed. Examination showed that streptococci were present and that the microorganisms found in the vagina were of the non-virulent order. He also describes the case of a patient who had fever after confinement, and who was treated by a physician by dilatation and curetting. Peritonitis developed, and the patient was brought to the clinic. On examination, hemolytic streptococci were present in the blood, and in the vaginal secretion hemolytic streptococci and the *Bacillus coli communis*. Extirpation of the uterus was

practised, and was followed shortly after by the death of the patient. On examination, peritonitis was present, hemolytic streptococci were found in abundance in the peritoneum, in the sinuses of the uterus, and throughout the circulation. Veit calls attention to the clinical rule that in the presence of actively virulent germs the physician should not disturb the uterus. In sapremia, and when the lower orders of bacteria only are found within the womb, decomposing material may be brought away to advantage. Microscopic and bacteriological examination of the secretions and fluids of the vagina gives valuable clinical information concerning the choice of operation. When the ordinary bacteria of putrescence are present, with fever and retention of placenta, the uterus should be emptied at once. When virulent streptococci are found in the vaginal secretion, but are not in the blood, the womb should not be disturbed. When the streptococci are not virulent, retained placental portions should be removed. When virulent bacteria are found in the blood and in the vaginal secretion, the prognosis for the patient is probably hopeless. The womb may be emptied or may be completely removed as a last resort.

**Relation Between the Time of Rupture of the Fœtal Membranes and Lacerations of the Cervix Uteri.**—COLYER (*Brit. Med. Jour.*, November 20, 1909) has studied in the General Lying-in Hospital of London 233 primiparous cases, in 164 of which vaginal examinations were made after labor. These examinations were made on the ninth or tenth day of the puerperal period, after thorough evacuation of the bowel and bladder. The conditions noted were the height of the fundus uteri above the pubes, the position of the uterus and the presence or absence of flexion, and the condition of the cervix, especially regarding the presence of lacerations. These were divided into three degrees: (1) Those extending less than half way up the vaginal cervix; (2) those reaching half way; (3) those extending to or beyond the junction of the vagina and cervix. In addition, the condition of the bases of the broad ligaments was studied to determine whether thickening of these tissues was present and to what extent. The character and quantity of the lochial discharge were also noted. In addition to these points, Colyer also sought to determine the relation between quality and quantity of the lochia, and the degree of uterine involution, the relation between the lacerations of the cervix and the condition of the involution, and also the relation between the cervical lacerations and thickening of the broad ligaments.

He was not able to establish a definite relation between the character of the lochia and the degree of involution present. Opinions differed as to a relation between the thickening in the broad ligaments and the degree to which the cervix was torn. Colyer was surprised to find that he could establish no relation between the lacerations of the cervix and the degree of uterine involution present.

He was able, however, to establish a relationship between the degree of dilatation of the os at the time when the membranes rupture, and the degree of lacerations of the cervix occurring during labor.

Five per cent. more severe lacerations occurred in cases, in which the cervix being thought by obstetricians to be dilated, the membranes were ruptured, than were observed in those cases in which the mem-

branes ruptured spontaneously and the cervix was subsequently found to be fully dilated. In cases in which the os was thought to be almost fully dilated, and the membranes were ruptured, deep lacerations occurred in 45 per cent. In those in which the os was not larger than a dollar, but 12.5 per cent. showed deep lacerations; but in every case in primiparous patients, in which the membranes were ruptured artificially, some laceration occurred.

An effort was made to consider the influence of the weight of the child and the diameters of the foetal head upon the occurrence of cervical lacerations, but it could not be established that a definite relation exists between the two.

He tabulates 164 cases, the average age of the patient being 23.17 years. In these, slight lacerations occurred on the right side in 49.39 per cent., upon the left side in 46.93 per cent. of cases. Moderate lacerations occurred upon the right side in 15.24 per cent., and on the left side in 17.07 per cent. of cases. Deep lacerations occurred on the right side in 6.09 per cent., and on the left side in 12.18 per cent. of cases.

Where the membrane ruptured spontaneously with the os fully dilated, there were 33 cases, the average age being 21.16 years. Of these, there were slight lacerations on the right side in 48.48 per cent. and the same percentage on the left side. There were moderate lacerations on the right side in 3.03 per cent., and upon the left side in 21.21 per cent. of cases. Deep lacerations upon the right side were found in 6.06 per cent., and upon the left side in 9.09 per cent. of cases. Where the membranes were ruptured artificially there were 46 cases, the average age of which was 22.8 years. These had slight lacerations on the right side in 54.34 per cent. of cases, and upon the left side in 41.32 per cent. There were moderate lacerations on the right side in 19.56 per cent., and upon the left side in 36.95 per cent. of cases. There were deep lacerations upon the right side in 6.52 per cent., and upon the left in 15.21 per cent. of cases.

Where the os was almost fully dilated and the cases had rupture of the membranes either spontaneously or artificially produced, there were 11 cases, the average age being 23.52 years. Of these, there were slight lacerations on the right side in 36.36 per cent., and on the left in 27.27 per cent. of cases. There were moderate lacerations on the right side in 36.36 per cent., and on the left in 18.18 per cent. of cases. There were deep lacerations upon the right side in 9.09 per cent. and on the left side in 45.45 per cent. of cases. Where the os was not larger than a dollar, the cases numbered 6, the average age being 21.5 years. These had slight lacerations upon the right side in 50 per cent., and on the left side in 75 per cent.; moderate tear on the right side in 25 per cent., on the left in 12.5 per cent.; deep tear upon the left side in 12.5 per cent. of cases.

The practical conclusion of this research is that artificial dilatation and premature rupture of the membranes should be avoided whenever possible in the conduct of labor. It is much better to allow spontaneous dilatation to occur, and to interfere promptly in the second stage of labor, than to complete dilatation artificially by the premature rupture of the membranes.

**The Position of the Patient during the Puerperal Period.**—A contribution to the literature of the puerperal period, criticizing the proposition to allow puerperal patients to get up early, is made by HICKS (*Brit. Med. Jour.*, November 20, 1909). He believes that women, as a rule, do not want to get up after labor much before the expiration of two weeks, and that women among the poorer classes commonly complain of their hardship in being obliged to resume the upright posture. Hicks believes that rest is indicated to secure through involution of the entire genital tract, and also to encourage the successful establishment and performance of lactation. He is of the opinion that rest, good food, and a happy state of mind will do more to prevent prolapse of the abdominal and pelvic viscera than the few days exercise which the patient will obtain by rising early.

Hicks does not believe that the assumption of the upright posture has any essential influence in the development of septic infection. He believes that the recumbent posture is favorable for drainage, and that straining from respiratory efforts and coughing will dislodge any clots which will accumulate in the upper portion of the vagina. He also does not believe that the upright posture helps to prevent backward displacements. In his view the pelvic diaphragm is overstretched, often torn and relaxed during labor, and the recumbent posture is necessary for its complete involution. If it remains without involution, he believes that the weight of the uterus and other abdominal viscera is thrown upon the pelvic floor, which increases venous engorgement and tends to produce retroversion, prolapse, and congestion. He believes that there is abundant clinical evidence that the uterus not only maintains its normal position more easily with the patient recumbent, but that a retroverted or prolapsed pregnant uterus will not, in nine cases out of ten, resume a normal position if the patient is not kept in a recumbent position. He further believes that the recumbent posture favors the relief of venous engorgement of the pelvic organs, and allows the supports of the uterus to resume their proper function.

## GYNECOLOGY.

UNDER THE CHARGE OF

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**The Pathology of the Red Degeneration of Uterine Myomas.**—SMITH and SHAW (*Jour. Obst. and Gyn. Brit. Emp.*, 1909, xv, 225) after a careful study of five specimens together with the cases connected with them, have decided that: (1) The chief change found in "red degeneration" of fibroids of the uterus consists in thrombosis of the bloodvessels. (2) This thrombosis and red coloration may commence at the periphery of the tumor. (3) The tumors are also in a state of degeneration,

as evidenced by a homogeneous material separating the muscle bundles in many places. (4) The tumors contain fat and fat crystals, probably derived from the breaking up of the muscle bundles. (5) The tumors are liable to become infected by septic organisms and so give rise to acute toxic symptoms. (6) Pregnancy is probably a predisposing factor in the causation of this condition.

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**Combination of Pfannenstiel's Transverse Incision and Shortening of the Round Ligaments in Operative Treatment of Complicated Retroflexio Uteri.**—RICHARD WERTH (*Zentralbl. f. Gynäk.*, 1909, xxxiii, 477) combines the transverse incision of Pfannenstiel extending well beyond the lateral borders of the recti with shortening and suture of the round ligaments in the inguinal canal opened subfascially by loosening the aponeurosis of the externus musculus. The incision should be made close to the symphysis, thus avoiding the necessity of extensive loosening of the aponeurosis of the external oblique at the inferior wound margin. The incision should be carried to within 2 or 3 cm. of Poupart's ligament. Werth makes the incision immediately above the inguinal canal, as it facilitates orientation and affords additional protection against possible future hernia.

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**The Operative Treatment of Extensive Cystocele and Uterine Prolapse.**—WATKINS (*Surg., Gyn., and Obst.*, 1909, viii, 471), in a paper read before the American Gynecological Society, described an operation he had devised and performed 68 times for extensive prolapse of the uterus and bladder. It is done as follows: The anterior vaginal wall is severed from the uterus by a transverse incision, and through this opening the bladder is separated from the vagina, and the vaginal wall then divided in the median line. The bladder is next separated from the uterus and the peritoneum opened. The fundus uteri is now brought in contact with the anterior end of the opening in the vaginal wall and sutured in that position. The flaps of the vaginal wall are sutured to the uterus and to each other. But one failure is known among the 68 patients. Various modifications are made if the procreative period is not passed and if the uterus is thought to be too large.

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**Epithelioma of the Uterus After the Menopause; Early Hysterectomy.**—REYMOND (*An. de gyn. et d'obst.*, 1909, xxxvi, 115) reported the cases with the accompanying specimens of 7 cases, in each of which the patient had had discharges of blood from the uterus some time after the menopause. One of them was a young woman, from whom the uterine appendages had been removed some time before. In every one of them palpation and specular examination had failed to find a lesion. In 4 of the 7 the lesion was in the body of the organ, in 1 in the isthmus, and in 2 in the cervical canal. Cancer was present in each. In one recurrence was noted at the end of four years.

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**Skin Metastases in Cancer of the Uterus.**—HEINRICH OFFERGELD (*Monatsschr. f. Geburtsh. u. Gynäk.*, 1909, xxix, 871), in reviewing the literature, compiled 27 cases of skin metastases in uterine cancer. A careful study of the cases showed that metastases of the skin and mammae

are rare in uterine cancer, and that they usually appear in advanced carcinoma. They occur most commonly in the region of the umbilicus and the mammae. They are of hematogenous, probably of lymphogenous, origin. Aside from other potent factors, the cause of occurrence of skin metastases may be attributed to the close relationship of the surface epithelium of the uterus to the epithelium of the body surface. Skin metastases, as a rule, do not give rise to clinical symptoms. Carcinoma of the distal portions of the urogenital apparatus, which usually arise through retrograde lymphogenous transport, although they may occasionally arise by way of the blood channels, occupy a special reservation as regards frequency and origin. They occur preferably after corpus carcinoma, but they also occur in carcinoma of the cervix, and in the earlier stages even. Their presence, however, does not indicate that the case is inoperable.

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**Atresia of the Vagina with Hematometra, Hematosalpinx, and Hematovarium.**—A. BROTHERS (*The Post-Graduate, 25th Anniversary Volume, 1908*), collected 164 cases of vaginal atresia and its consequent blood accumulations occurring during the past twenty years. Spontaneous rupture or evacuation occurred in 10 of primary blood retentions and in one secondary blood retention. Probably none of them was associated with hematosalpinx. When the last mentioned condition existed a considerable mortality rate has been present. Of 19 cases of this sort, 4 died of or shortly after operation by the abdominal route. In 10 cases the operation was successfully performed by the vaginal route.

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**Ureteral Fistulas as Sequels of Pelvic Operations.**—In quite an exhaustive paper (*Surg., Gyn., and Obst., 1909, viii, 479*) SAMPSON discusses ureteral fistula following pelvic operations, again emphasizing the importance of retaining the sheath of the ureter and of avoidance of injury to the blood supply of that duct. Reference is made to the changed relations of the ureters and uterus that are produced by displacements of the latter, either during or independent of surgical operations on these structures. Particularly is attention requested to such etiological factors in this respect as lateral displacement of the cervix uteri, the presence of appendages involved in inflammatory masses, and intraligamentary tumors. It is a notable fact that Sampson does not recommend the employment of the ureteral catheter or bougie as a prophylactic procedure. Sampson's advice regarding nephrectomy for ureteral fistula in which renal infection has ascended from a ureteral fistula is sound and indirectly is a strong argument for early surgical treatment of such fistulae.

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**Necrosis of Fibromyoma of the Gravid Uterus as an Etiological Factor in Occlusion of the Intestinal Tract.**—SPERANSKY-BACHMETEW (*Zentralbl. f. Gynäk., 1909, xxxiii, 553*) reports a case of intestinal occlusion caused by necrosis of a fibromyoma of a pregnant uterus in a primipara, who presented the typical symptoms of loss of patency of the intestinal canal. Artificial interruption of pregnancy was not followed by improvement. Celiotomy was done. A pediculated uterine tumor was found beneath



the transverse colon; it was adherent to the great omentum; the latter was ligated off and separated. The adhesions to the sigmoid flexure were separated and the tumor removed by a wedge-shaped incision into the uterus. Uninterrupted recovery followed. The tumor was found to be a fibromyoma that had undergone hyaline degeneration and necrosis at the point where it had come in contact with the intestine. The growing uterus drew up the tumor with the adherent intestine, causing the short mesentery to exert an opposite or downward traction; constipation increased the meteorism, while prolapse of the descending colon augmented torsion.

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**Thrombophlebitis with Peroneal Neuritis and Paralysis Following Supravaginal Hysterectomy.**—R. PETERSON (*Surg., Gyn., and Obst.*, 1909, viii, 517) reports a case of this kind which is employed as a basis for discussion. The peroneal palsy is attributed to either trauma or pressure upon the lumbosacral cord. The latter may be caused by an inflammatory process, and this often may arise from thrombosis; and if this process be considerable at the crossing of the left internal iliac vein and the lumbosacral cord, peroneal neuritis may result.

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**Experimental Studies of Postoperative Peritoneal Adhesions.**—G. GELLHORN (*Surg., Gyn., and Obst.*, 1909, viii, 505) considers the problem of postoperative peritoneal adhesions from the standpoint of treatment resolves itself into two captions, viz., prevention of their formation and prevention of their again forming if separated. Under the first heading Gellhorn states the most rigid asepsis possible should be employed, raw surfaces and pedicle stumps should be covered by peritoneum or grafts of omentum, and the *en masse* ligature abandoned. Dry air contact should be avoided by moist asepsis and rapidity employed if possible. Avoidance of excessive manipulation of the peritoneum and proper bowel preparation and posture are considered important desiderata. Gellhorn emphasizes the necessity for careful replacement of the abdominal contents after intra-abdominal work, pouring hot salt solution on them at the time, and the early use of the high enema during the first twelve hours after the end of the operation, in conjunction with catharsis. In the consideration of preëxisting adhesions Gellhorn groups the subjects into: (1) Those adhesions formed from ectopic pregnancy, (2) those from peritonitis, and (3) those from former operations. Gellhorn insists the first group leaves no lasting adhesions, and that in the two other groups permanent adhesions result. Reference is made to the experiments made by others before Gellhorn describes his experiments with lanolin, which were not productive of favorable results.

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**New Method of Shortening the Round Ligaments in Retroversion of the Uterus.**—J. JERIE (*Zentralbl. f. Gynäk.*, 1909, xxxiii, 686) reports a new method of shortening of the round ligaments which he employed successfully in several cases of retroverted uterus. His method, in brief, consists of an incision in the linea alba 7 cm. in length, careful inspection of the uterus and adnexa, and eventual breaking up of adhesions or operation, if necessary, for the removal of diseased adnexa. The round ligament is grasped with artery forceps, 6 to 10 cm. removed from the

horn of the uterus, and an incision 1 cm. in length is made in the anterior fold of the broad ligament at a distance of 2 cm. from the ligamentum rotundum. Through this incision a small artery forceps is introduced between the two folds of the broad ligament, grasping the round ligament, which is drawn out after having been freed from the surrounding connective tissue. The artery forceps first applied to the round ligament is now removed. The uterus is next grasped by the hand or bullet forceps and held while the upper muscular layers of the anterior aspect of the uterine cornu are undermined for a width of about 1 cm. with a narrow, two-edged knife, thus creating a canal, into which an artery forceps is then introduced. The isolated loop of round ligament is grasped by this forceps and drawn through the canal until it becomes visible on the mesial end of the canal, where it is fastened with a strong catgut button suture, transfixing the undermined piece of muscle, the round ligament, and the uterine wall proper. In addition a catgut button suture is placed at each end of the muscle bridge encompassing the uterine wall, one arm of the loop of round ligament, and the undermined muscular bridge. The peritoneum over the round ligaments will usually approach the muscle bridge and cover the loop of the round ligament completely. At times a small catgut suture may be necessary, however. The other side is operated upon in the same manner. The shortened round ligament is re-implanted into the uterine muscle itself at almost the same site of the original attachment, and the uterus remains in the small pelvis in correct position.

## OPHTHALMOLOGY.

UNDER THE CHARGE OF

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**Spirochæta Pallida in Syphilitic Eye Lesions.**—CORBUS and HARRIS (*Ophthal. Rec.*, June, 1909, 294) have examined some 200 cases of specific lesions primary and secondary. They conclude that *Spirochæta pallida* is present in all syphilitic lesions, including those of the eye. In chancres and mucus patches the diagnosis should be made by the demonstration of the spirochete. All other lesions of the eye of syphilitic origin may be diagnosticated by means of the Wassermann test, as may also ocular lesions depending upon pathological changes in the nervous system of syphilitic origin. The same test should be applied in cases of suspected syphilitic origin. The Wassermann test depends upon the discovery of Bordet and Gengou, that bacteria or their extracts will unite with their corresponding antibodies by means of complement and fix it. (Complement is present in all sera. What it is, is not definitely known. It may be conveniently obtained from the blood of guinea-pigs.)

**Acoïn.**—BRUNETIERE (*Clin. ophthal.*, July 10, 1909, 326) recommends subconjunctival and intramuscular injections in 1 per cent solution. The analgesic effect, although inferior to that of cocaine, is much more prolonged and entirely free from risk. Acoïn is quite unstable and forms insoluble precipitates with most medicaments in solution; such chemical alterations diminish the analgesic properties of the drug; hence, to obtain the maximum effect in subconjunctival and intramuscular injections, it is advisable to inject first the solution of acoïn, followed after an interval of one or two minutes by the medicament desired. Acoïn may also be employed dissolved in oil, but this vehicle does not appear to be superior to aqueous solutions.

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**Normal Flora of the Rabbit's Conjunctiva.**—TCHIRKOWSKY (*Annal. d'oculist.*, April, 1909, 291) finds that the flora of the normal conjunctival sac of the rabbit presents a great variety of forms, and differs from that of man by the rarity of bacilli in aggregation. Both aërobic and anaërobic forms are present, among which some are of undoubted pathogenic effect upon the eye (*Bacillus perfringens*). The pathogenic power of the microbes which occur there most frequently is, however, inconsiderable; it is only under particularly favoring conditions, especially by the introduction of large numbers into the vitreous body, that the germs develop rapidly and entail destructive consequences to the organ.

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**The Etiology of Refractive Anomalies and Emmetropia.**—STRAUB (*Zeit. f. Augenheilk.*, 1909, xxii, 236) observes that, in view of its overwhelming frequency, emmetropia has been assumed to be the normal refraction. But when the fact is taken into consideration that the eyes of the newborn are mostly hyperopic, while emmetropia, notwithstanding decided variations in the structure of individual eyes, is attained with great exactness in the adult and that only a minority of emmetropes become myopic during adolescence, one must assume some mechanism which guides the increase in the refraction of the newborn that emmetropia shall result, and which shall govern the eyes having arrived at emmetropia so that the majority shall not become myopic. Straub terms this mechanism "emmetropization." Emmetropization assumes that length of axis and lenticular refraction shall be so related that emmetropia shall result. Of these two factors, the lenticular refraction is the predominant. If the shape of the lens was brought about by two antagonistic muscles, the explanation would be apparent. Clonic contraction of the muscles would then cause positive and negative accommodation, while tonic contraction of the antagonists would determine the shape of the lens in repose. The tone of the ciliary muscle can only increase the refraction, not diminish it. The intra-ocular tension tends to give the eye a spherical form. The circular groove between the cornea and sclera opposes this tendency. The most elastic tissue would be unable to withstand such continuous pressure permanently. Muscle alone can offer constant resistance, and this is furnished by the circular portion of the ciliary muscle. It is the cause of the groove. The intra-ocular tension is the antagonist required; it is this which tends to smooth out the curve in consequence of which also the lens is flattened and the refraction diminished; the ciliary muscle by its tonic contraction

opposes such flattening and is the force which determines adaptation for distance. Such tonic contraction leads in the developing eye to permanence of structure of the form of the ciliary muscle, so that the length of the muscle which was in the beginning a dynamical factor becomes static. A slight degree of tone persists in the majority of eyes. An important practical question relating to the development of myopia arises in connection with these views. In such eyes also which have departed from emmetropia the *visus* to adaptation for distance had also been active, but it has been overcome, the axis has increased in length. If the optical condition of emmetropia has been restored by fully correcting glasses, the mind has been given renewed opportunity to put in play the mechanism of emmetropization so that a psychic factor is the principal role in the efficacy of full correction. The emmetropia thus furnished will only be permanent in cases in which the subject manifests a desire to see clearly at a distance. If such desire is not present, the correcting glasses will not prevent the myopia from progressing. Loss of tone of the ciliary muscle diminishes the resisting power of the ocular walls and permits enlargement of the myopic eye. Full correction increases the power of the ciliary muscle in that it stimulates the accommodation.

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**Malignant Growths of the Frontal Sinus.**—In reporting a case of this rare affection, SNEGIREFF (*Klin. Monatsbl. f. Augenheilk.*, 1909, 622) insists that there is no early symptom which differentiates a malignant growth from other affections of the frontal sinus, such as empyema or polyp. Prominence of its wall with consequent displacement of the eyeball and double vision, impairment of the sight, and pain are symptoms common to different conditions. The diagnosis cannot be made with certainty so long as the posterior wall is still intact, the meninges uninvolved, the growth limited to its original seat, etc.

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**Treatment of Strabismus by Operation upon the Non-squinting Eye.**—BETREMIEUX (*Annal. d'oculist.*, 1909, 53) again urges tenotomy of the non-squinting eye. He argues that the fixing eye, by reason of the synergy of the lateral movements, can only maintain its proper position by exaggerating the deviation of its congener; after a moderate tenotomy of its internus, it readily conserves the correct position but this is only possible on condition that its congener does the same. He thinks that if Donder's theory is correct, operation upon the non-squinting eye is logical.

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**The Inner Pole Magnet.**—MELLINGER (*Archiv. d'ophthal.*, 1909, 193) objects to the giant magnets usually employed, that the lines of force are too strongly divergent, tending as they do to join the opposite pole, so that the foreign body within the eye which must be magnetized by these same lines of force, is only affected by a small part of them—a disadvantage the more marked in proportion as the foreign body is lodged deeper within the eyeball. To compensate this loss, the transverse section of the iron bar may be augmented, but such increase in size interferes with facility of manipulation. In order to diminish this loss, Mellinger has had constructed a large solenoid with several hundred windings of wire of such size that the head may be placed

at its centre; upon the passage of an electric current through this a homogeneous magnetic field is produced the greatest density of which lies at the bisection of the axes of the solenoid. Here the lines of force are nearly parallel to the axis. Bits of iron brought to this spot are at once magnetized to saturation. When an iron rod is brought within the influence of the magnet, it as well as the foreign body within the eye becomes magnetic; the degree of magnetization is proportionate to the size of the rod, so that the effect can be graduated by varying the size of the latter, and too rapid issue of the foreign body may be avoided. By the employment of currents of varying intensities, the operator has complete control of the attractive force he wishes to use.

## PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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**The Pathogenesis of Pernicious Anemia.**—GRAFE and RÖHMER (*Deut. Archiv f. klin. Med.*, 1909, xcvi, 397) endeavored to isolate a hemolytic substance from the stools of patients suffering with ulceration of the intestines. They studied the stools from this point of view from 106 cases, all but 11 of which showed some gastro-intestinal lesion. A hemolytic substance was most constantly found in the stools of patients suffering with tuberculous enteritis (10 out of 11 cases), while normal cases gave practically negative results. In catarrhal jaundice, in liver diseases, and in cholecystitis positive findings were obtained in all 6 cases. In typhoid fever 113 experiments were done, 26 of which were positive in 45 experiments in the fastidium of the disease, 9 positive in 32 toward the close of the attack (*Stadium decrementi*), and 8 were positive in 36 experiments during convalescence. Grafe and Röhmer believe that the hemolytic substance appears in the stools whenever there is a disturbance of fat absorption, and they consider it necessary to exclude diarrhoea and fatty stools in order to determine by this method anything in regard to the state of the intestines. They do not consider, however, their results sufficiently established to be of any diagnostic importance, but they hope to determine how much ulceration is necessary to produce the lipoid hemolytic substance.

**Application of the Deviation-of-Complement Test to the Detection of Albuminous Substances in the Urine.**—C. H. WILSON (*Jour. Path. and Bact.*, 1909, xiii, 484) has found that very minute quantities of albumin may be detected in the urine by means of the deviation-of-complement

test. For antigen he has used the serum of rabbits which had been immunized against human blood serum. When albuminous urines were diluted to such a point that they no longer gave a reaction with heat and acetic acid or with nitric acid, they still yielded positive results by the complement-deviation test; while in many instances albumin could be detected by this method in diluted urine when it could not be demonstrated by the ordinary chemical tests. The deviating power of the urine is not affected either by filtration through a Berkefeld filter or by dialysis. The antibody of the urine was, moreover, found to reside entirely in the serum albumin and serum globulin, and after the removal of the substances from the urine the remaining fluid no longer had the property of an antibody. Wilson believes that by this method one may detect minute quantities of albumin in the urine, which cannot be demonstrated by any other means. The experiments show further that the albumin which occurs in the urine in nephritis and other conditions is native albumin, and not, as has been suggested by some observers, a proteid constituent of the food which has passed unaltered. Most of the conclusions in regard to this so-called alimentary albuminuria have been drawn from experiments made by means of the precipitin reaction; and it was claimed by Ascoli in particular that egg albumin after ingestion could be found in the blood serum and in the urine. That albuminuria may occur after eating large quantities of raw eggs is well known, but recently Wells has shown by means of the anaphylaxis reaction that the albuminuria in such cases is due to the presence of true serum albumin. Guinea-pigs sensitized with urine from four healthy persons with experimental albuminuria, produced by eating raw eggs, and with the urine from two cases of nephritis, reacted typically and severely to subsequent injections of human aseptic fluid and not at all to egg white or egg albumin.

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**Recent Investigations upon Trypanosomiasis.**—EHRlich (*Arch. f. Schiff's-und. Tropen-hyg.*, 1909, xiii, 91) sums up the most recent investigations upon trypanosomiasis, which have been made in his laboratory. One of the obstacles encountered in the therapeutic use of certain drugs in experimental trypanosomiasis is the gradual immunization of the parasite against the drug. By treating animals infected with trypanosomes repeatedly with certain preparations of arsenic it has been possible to obtain a variety of trypanosomes which is proof against that particular drug. This acquired property is retained through many generations, as many as 400 in one instance, and over a period of four years. The development of this arsenic-proof variety of parasite takes place, according to Ehrlich, in the following manner: The parasites contain, as do all other cells, certain chemical receptors, which Ehrlich terms chemoceptors and which have a specific affinity for the arsenic radical. By the union of these receptors with the arsenic radical the toxic effect of the drug upon the parasite is possible. By repeated injections of arsenic this receptor becomes saturated and can no longer bind the drug. Not only can arsenic-proof varieties be obtained, but a variety which is refractory to immune serum. The production of this immunity is, however, somewhat different from that just described. It has also been possible to cultivate through many generations in animals parasites which show a fairly specific resistance to other substances

besides arsenic. Parasites made proof against pyronin, however, are also proof against the arsenic preparations. This demonstration is of great practical value. Experiments upon the method by which the arsenic preparations cure an animal infected with trypanosomes go to show that the drug does not destroy the parasites but renders them incapable of reproduction. It was surprising to find that when arsenic-proof varieties were treated in vitro with weak solution of arsenic preparations their motility was stopped in three to seven minutes, whereas the ordinary varieties remain active for fifty minutes. This observation led to the discovery through other experiments that one portion of the parasites, that which is intimately connected with the motility, is readily susceptible to arsenic, while the substratum, which is connected with reproduction, is hyposcnsitive to arsenic preparations.

Among the arsenic preparations that have been used, it has been found by WENDELSTADT (*Berl. klin. Woch.*, 1908, No. 51) and ROEHL (*Zeit. f. Immunitätsforschung und exp. Therapie*, 1909, i, 1) that arsenophenylglycin is the most powerful against the parasite and least toxic to the host. Mice and guinea-pigs in the last stages of infections have been cured by a single dose. Moreover, this drug has proved more effective against the varieties proof against other forms of arsenic than any other preparation. The drug must be preserved *in vacuo*, for on exposure to air it rapidly oxidizes to form a highly toxic product. It has great advantages over atoxyl, arsacetin, and orsudan. The drug has already been used in Africa and double doses of 0.75 and 1 gram have been given without ill effects to the patient. Arsenophenylglycin may be made even more effective in animals by administering at the same time trypanosan by the mouth. Most brilliant results have thus been obtained in experimental trypanosomiasis, and the outlook for a similar therapy in man is most hopeful.

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ORIGINAL ARTICLES.

THE TREATMENT OF ACUTE OTITIC MENINGITIS.

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OF the various complications of purulent otitis media, otitic meningitis has been the one condition most difficult of diagnosis and least amenable to surgical treatment. The symptoms of the disease are often obscure, and no definite plan of surgical procedure has yet been outlined which will enable the surgeon to bring the case to a favorable termination. Owing to the magnitude of the subject under discussion, our distinguished colleague, Dr. Lermoyez, has consented to consider simply the diagnosis and symptomatology of otitic meningitis, and has courteously left to me the task of speaking to you on the subject of the treatment of this important condition.

The treatment of an otitic meningitis depends very largely upon the character, location, and extent of the meningeal inflammation. For this purpose, therefore, I will divide our cases into certain groups: (1) Those cases involving a limited area of dura alone, that is, cases of extradural or epidural abscess. (2) Those cases in which a general meningitis is present. These cases may be divided into (*a*) a serous meningitis involving principally the subdural space, and (*b*) a serous meningitis involving both the subdural space and the lateral ventricles. (3) Cases of purulent meningitis, involving the subdural space over a localized area. (4)

<sup>1</sup> Read at the Eighth International Otological Congress, held at Budapest, August 29 to September 4, 1909.

Cases of general purulent meningitis, involving both the subdural space and the lateral ventricles.

With the assistance of one of my confrères, Dr. Charles E. Perkins, I have collected from literature 101 cases of otitic meningitis of various forms. Of these cases, 45 were cured and 56 died. Of the cured cases, 34 were cases of serous meningitis, 4 were cases of circumscribed purulent meningitis with serous meningitis, and 4 were cases of circumscribed purulent meningitis; diffuse purulent meningitis occurred in 3 cases. Of this series of cases, the operative procedures instituted for their relief were sufficiently interesting to be reported somewhat in detail, in that they afford us certain data for formulating the treatment in similar conditions.

It is worthy of note that in 6 of the cases all that was necessary to relieve the meningeal symptoms was first to clear out the local focus of infection by means of either the simple mastoid operation or the complete radical operation, and second, to relieve, temporarily, the increased intracranial pressure by lumbar puncture. In most instances, however, the operative treatment was more complex, and consisted, first, in thoroughly clearing out the site of infection, either by means of the radical operation or the simple mastoid operation, as circumstances might demand; that is, the radical operation was performed when the condition followed a chronic purulent inflammation, while in those cases following an acute otitis media the simple mastoid operation was all that was necessary. In addition to the treatment directed to the site of primary infection, in 9 cases an epidural abscess was evacuated. In 4 cases simple exposure of the dura, with lumbar puncture, relieved all the meningeal symptoms. Drainage of the lateral ventricle was performed 7 times, and in one of these cases the fluid evacuated from the ventricle was purulent. In 18 cases the dura was incised, and in 5 of these the dural incision evacuated a purulent fluid. In 3 cases the meningeal symptoms followed a sinus thrombosis, and the jugular was excised for the relief of this condition. It is especially noteworthy, in reviewing this series of cases, to remark that in 20 cases out of 45, lumbar puncture was performed, and that this procedure seemed in no small way to contribute to the successful result of the other operative measures.

Going over my own statistics of meningitis, I find that I have operated on 65 cases of otitic meningitis, of all varieties. In 54 of these cases the meningitis was of the most simple variety, that is, a circumscribed purulent pachymeningitis, and of these 54 cases, 48 recovered and 6 died. Death was due in 1 case to septic pneumonia, in 1 case to diabetes, 1 case died of cerebellar abscess, and 3 cases died of general meningitis. These personal statistics show, therefore, that a localized meningitis, promptly treated, is a complication of no special gravity—that there is little ten-

dency for it to extend to the general meninges, and that if properly treated, the case will almost invariably terminate favorably. Eleven of the cases operated upon were cases of general meningitis. Of these, 3 recovered and 8 died. The cases which recovered were all of the serous variety.

I will now consider the various operative procedures which were instituted in these cases for the relief of the condition. In cases in which a simple localized meningitis is present, and in which this inflammatory process involves simply the dura, all that is necessary is first to clear out the local site of infection, either by the complete mastoid operation, in cases following an acute otitis media, or the radical operation in cases following a chronic purulent middle-ear inflammation. This operative procedure must be complete, if beginning meningeal symptoms are to be controlled. Every vestige of diseased bone must be removed. When, during the operation, a collection of pus is found between the dura and the bone, it is necessary to remove completely the bone overlying the infected dura. It is important, however, that the removal of the bone should not extend beyond the limits of the extradural abscess. The extent of the dural inflammation is usually well defined by adhesions which develop between the dura and the bone, about the margins of the abscess. The bone should be removed to the very edge of these dural adhesions, but not beyond this point. The surface of the dura is usually covered with granulation tissue, this granulation tissue varying in thickness according to the duration of the inflammatory process. It has been my practice to curette this granulating dural surface very gently, so as to remove all necrotic tissue, while, at the same time, the healthy granulation tissue is disturbed as little as possible. Care must be taken not to use the curette too forcibly, as frequently the subdural space is separated from the abscess cavity by an extremely thin layer of dura, and too vigorous use of the curette might open the subdural space and lead to a fatal leptomeningitis. Necrotic granulations, therefore, should be removed carefully, while healthy granulations should be left. After the entire abscess cavity has been thoroughly exposed, it should be packed with iodoform gauze. The subsequent management of the case requires no special description.

In cases in which the meningeal inflammation involves either the subdural space, the lateral ventricles, or both, the operative procedures must vary according to the extent of the meningitis and its character, that is, as to whether the meningitis is confined chiefly to the subdural space or whether it involves the ventricles as well, and secondly, as to whether it is of the serous or purulent variety.

In the 11 cases of general meningitis upon which I have operated, as before stated, 3 terminated favorably. The procedure in one of these cases consisted simply in draining the extradural space and making a free incision in the dura over the involved

area, thus relieving pressure in the subdural space. In a second of these cases the complete radical operation, with free opening of the superior and external semicircular canals, was followed by a cure. In the third case, complicated by a temporosphenoidal abscess, symptoms of serous meningitis came on after the evacuation of the abscess. In this case, incision of the dura, lumbar puncture, and drainage of the ventricle were followed by complete recovery.

From my own series of cases, together with those which I have collated from literature, it seems that we may be in a position to formulate somewhat exactly the treatment of this condition, which has, up to the present time, caused so much trepidation among otologists. First and foremost, should be placed the prophylactic measures. Every acute middle-ear inflammation should be treated along modern surgical lines—by early and free incision of the drum membrane, thus affording a prompt evacuation of the products of inflammation in the tympanic cavity, and lessening the possibility of extension of the inflammatory process inward to the cranial cavity.

Secondly, when the inflammation has extended to the cranial cavity, producing symptoms of meningitis, the first indication is thoroughly to eradicate the primary focus of infection by performing either the complete mastoid or the complete radical operation, as the case may be. It has been conclusively proved by postmortem examination that the most common site of extension of an inflammatory process from the middle ear to the meninges, is through the labyrinth: consequently, whenever meningeal symptoms appear, a careful examination should be made to discover any fistulous tract in the external labyrinthine wall. These fistulæ are most common in the horizontal semicircular canal, although infection may take place through the superior or the posterior semicircular canals or through the oval window. In cases in which the labyrinth is involved, thorough drainage of the labyrinth is imperatively indicated. This is best secured by enlarging any fistulous tract which may be found in the semicircular canals, the tract being enlarged toward the vestibule, so as to secure complete drainage. If the infection has occurred through the oval window, the vestibule should be drained in this region by enlarging the oval window downward and forward, so as very thoroughly to drain the cochlea. After cochlear drainage is instituted, the vestibule should also be drained behind and above the facial ridge by opening the external semicircular canal. In one of my own cases drainage of the vestibule through the horizontal and superior semicircular canals was all that was required.

If the meningeal symptoms are pronounced, and indicative of increased intracranial pressure, lumbar puncture should be performed at the same time that the middle-ear cavity is exenterated.

Many have questioned the value of lumbar puncture as a therapeutic measure. In one of my own cases, and in two reported by my

distinguished colleague, Dr. Lermoyez, at the last International Otological Congress, this measure certainly was of distinct therapeutic value. I believe that, in all cases in which meningeal symptoms are pronounced, lumbar puncture should be performed, not only as a diagnostic measure, but as a means of relieving temporarily, at least, the intracranial pressure. From 20 to 40 c.c. of cerebrospinal fluid may be withdrawn, the amount of fluid taken away depending very largely upon the degree of intradural pressure. Care must be taken not to withdraw the fluid too rapidly, as too sudden relief of pressure may be followed by a hemorrhage into the brain substance. In some cases repeated lumbar puncture must be performed, the operation being repeated whenever there is evidence of increased intracranial pressure, as indicated by a low pulse rate, beginning choked disk, stiffness of the neck, or other similar symptoms.

In cases in which the meningeal symptoms are exceedingly pronounced, more radical measures may be demanded at the time of the first operation. In other words, the invasion of the meninges may have been so rapid that the removal of the primary focus of infection and the reduction of intracranial pressure by lumbar puncture may not be sufficient. We must also remember that in a certain number of cases of sudden increase in intracranial pressure, the foramina of Monro and the foramen between the third and fourth ventricles, may be blocked, thus preventing the escape of ventricular fluid into the spinal canal. In such cases lumbar puncture would not relieve the symptoms. In cases, therefore, in which the meningeal symptoms are extremely urgent, it is wise at the time of the primary operation to relieve the intracranial pressure by means of a decompression operation. This operation would naturally be indicated on logical grounds, and its efficiency is borne out by the statistics which I have collated. In 18 of the 45 cures already mentioned the dura was incised. Incision of the dura, therefore, should be performed in all cases in which meningeal symptoms are pronounced.

My own practice, in cases of this character, is as follows: The squama is exposed by an incision extending from the upper extremity of the ordinary incision made for exposing the mastoid, upward, and then forward and downward to a point just behind the external angular process of the frontal bone. This incision extends through the integument, the temporal fascia, and the temporal muscle. The musculocutaneous flap is then pushed downward and the middle cranial fossa entered just above the zygoma by means of a gouge. The opening in the cranial cavity is rapidly enlarged by means of the rongeur forceps, forward, upward, and backward, so as to expose the temporosphenoidal lobe over an area of, at least, three inches in longitudinal measurement and two inches in vertical measurement. The base of the temporosphenoidal lobe should



also be exposed by extending the opening in the squama downward and backward, so as to remove the roof of the middle ear and the roof of the mastoid antrum. The dura is next incised. It is a matter of preference as to whether the dura is incised vertically or longitudinally. Personally, I prefer to open the dura by two crossed incisions of about one and one-half inches in length. These incisions serve two purposes: first, they thoroughly drain the subdural space, and second, if there is a collection of fluid, either serous or purulent within the lateral ventricles, they allow the brain substance to expand outward, thus relieving the intracranial pressure. The operation is exactly analogous to the one performed in cases of inoperable tumors of the brain. It is my practice to pack about the margin of this incision with iodoform gauze, so as to secure drainage of the subdural space, and at the same time to cause a certain amount of amalgamation between the two layers of the pia, in case the subdural collection of fluid is small and the intraventricular collection large. I do not think it wise, as a rule, to open the lateral ventricle at the time of the decompression operation. The relief of intracranial pressure which follows incision of the dura will ordinarily be sufficient to relieve the urgent symptoms, and the ventricle can then be opened subsequently.

While decompression over the temporosphenoidal lobe is of undoubted value in certain cases, it may also be necessary to perform a similar operation over the cerebellum. This is best performed by making a horizontal incision from the superior extremity of the mastoid incision, directly backward to the median line. The incision may then be carried downward for an inch or an inch and a half, dividing all the soft tissues down to the bone. In this way a musculocutaneous flap can be reflected downward, exposing the cranium over the region of the cerebellum. As in operations of this character the operator would have already exposed the dura covering the lateral sinus, it is only necessary to enlarge the opening in the bone backward and downward by means of the rongeur, to the median line, in order to expose the cerebellar dura over a large area. Two incisions, crossing each other at right angles, should then be made through the cerebellar dura, exactly as described in considering the decompression operation over the temporosphenoidal lobe. Incisions through the dura, for the relief of intracranial pressure, have been of unquestionable value.

Regarding the value of drainage of the lateral ventricles, these were drained seven times in the forty-five cases which were cured, and in one instance the lateral ventricles contained pus. I have performed drainage of the lateral ventricle in three cases, with one recovery, and drainage of the fourth ventricle in two cases, both of which terminated fatally. It is interesting to note that in one case, in which the fourth ventricle was drained, the patient lived ten days after the operation, and finally died of a hemor-

rhage into the spinal canal. So that drainage of the fourth ventricle, through the cerebellar substance, is a procedure which may possibly be of value in these cases.

In establishing ventricular drainage, the best procedure, according to my opinion, after incising the brain substance and entering the ventricle, is to pass two very thin-bladed retractors into the ventricle, and, by separating these retractors slightly, gradually to evacuate the ventricular fluid. A folded rubber-tissue drain can then be inserted between the retractors, the retractors removed, and the drain left in position. This effects a slow and regular drainage of the ventricle, and is, I think, preferable to the use of either a gauze drain or a drainage tube.

Regarding the technique of the decompression operation, some operators, notably Cushing, of Baltimore, prefer to do what is termed an "intermuscular" operation. The incision through the integument is made in exactly the same manner as the one previously described. This incision, however, extends only through the integument. The margins of the incision are elevated by dissection. The temporal fascia is next incised in the same way, and this, together with the integument, is reflected from the underlying temporal muscle. The fibers of the temporal muscle are then separated longitudinally, so as to expose the squama. The periosteum is now divided, the middle cranial fossa entered through the squama, and the opening enlarged beneath the temporal muscle. The advantage of this procedure lies in the fact that the temporal muscle is not divided, and consequently, there is less danger of hernia cerebri.

As, in cases of otitic meningitis, we are dealing with an acute process, the necessity of doing an intermuscular operation for the relief of pressure is much less than in cases of increased intracranial pressure due to brain tumor.

I believe, in the cases now under consideration, that the operation as described by myself is rather better than the intermuscular method, as it can be performed much more rapidly. In the same manner, the decompression operation over the cerebellum may be performed by the intermuscular method, the first incision dividing simply the skin and superficial fascia. The muscular fibers covering the skull over the cerebellum may then be separated and the overlying bone removed, in the manner already described. In this region, also, I believe that the intermuscular operation possesses no advantages.

As we know, both from clinical experience and postmortem examination, that one of the most frequent avenues through which the meninges become invaded is the labyrinth, and as the subdural space communicates with the labyrinth through the aqueductus vestibuli and aqueductus cochleæ, it has seemed to me that, in certain cases of otitic meningitis which come on suddenly, good

results might be obtained by opening the cranial cavity in the region where the aqueductus vestibuli and aqueductus cochleæ open into the subdural space. These canals open into the subdural space on the posterior surface of the petrous pyramid, the aqueductus vestibuli entering the subdural space just in front of the lateral sinus and behind the internal auditory meatus on the posterior surface of the petrous pyramid, while the aqueductus cochleæ opens into the subdural space on the lower margin of the posterior surface of the petrous pyramid, just below the internal auditory meatus. The subdural space, therefore, could be opened in this region by incising the dura in front of the lateral sinus. Where the sinus is far forward, it is difficult to gain space enough to do this without risk of injury to the facial nerve. In the majority of cases, however, there is space enough in front of the lateral sinus to make a vertical incision three-quarters of an inch in length, through the dura, while a horizontal incision three-eighths of an inch in length could be made in most cases. Access could thus be gained to the posterior surface of the petrous pyramid and the subdural space drained at the very site of infection.

In cases, therefore, in which the meninges have been infected through the labyrinth, it may be found wise to drain the subdural space in this region, rather than posterior to the lateral sinus. I certainly think that in some of the cases in which otitic meningitis develops very rapidly, drainage of the subdural space in this region is, at least, worthy of a trial.

I may sum up, then, the surgical treatment of the disease under consideration, as follows:

1. The surgeon should always remove the primary focus of infection, either by the complete mastoid operation or the complete radical operation, according as the disease is dependent upon an acute or chronic middle-ear suppuration. At this time, any extradural collection of pus should be thoroughly evacuated.

2. Any fistulous openings in the outer wall of the labyrinth should be enlarged and the labyrinth drained by opening the semi-circular canal, vestibule, and cochlea.

3. With symptoms of moderate intracranial pressure, lumbar puncture should be performed to relieve this pressure.

4. With symptoms of severe intracranial pressure, or in cases of moderate intracranial pressure, when lumbar puncture is negative, a decompression operation should be done, either over the temporosphenoidal lobe or over the cerebellum, or in both situations.

5. If the symptoms are extremely urgent, the lateral ventricle may be opened at the time of the decompression operation. Preferably, however, the opening of the ventricles should be delayed for from twelve to twenty-four hours, in the hope that incision

of the dura may relieve the tension temporarily, and that the effused fluid may be absorbed.

6. In cases in which the infection seems to have travelled through the labyrinth to the subdural space, drainage of the subdural space on the posterior surface of the petrous pyramid, in the region of the aqueductus vestibuli and aqueductus cochleæ, should be instituted.

These comprise our various measures for the surgical treatment of acute otitic meningitis. Whether, at some later day, serum therapy may come to our aid in the treatment of otitic meningitis is, of course, open to question. The brilliant results which have been already attained in cases of epidemic cerebrospinal meningitis, by the use of the antimeningococcic serum, may lead us to believe that at some future date an injection into the spinal canal of a serum antagonistic to the particular germ causing the meningitis might be of value. A few cases have been treated with antistreptococcic serum. The results, however, are too uncertain and the number of cases too small to allow any definite opinion to be given on this subject at present.

## SOME POINTS IN THE TREATMENT OF CHOREA IN CHILDREN.

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CHOREA is a common disease of childhood, and in certain districts it is very prevalent. We see it in many phases—from the very acute maniacal form to the mild or chronic varieties, which may last for months. The treatment of chorea, while generally satisfactory, is sometimes a matter of difficulty, and the disease may effectually baffle the resources of the practitioner. When we consider that in many instances chorea is a rheumatic manifestation (and there is considerable proof that it is entirely so), that the child suffering from this disease may be subjected to much teasing, and may be punished unjustly, it is evident how important it is that prompt and appropriate treatment should be enforced.

REST. The first point in the treatment of patients suffering from chorea is rest, and without rest any other treatment will be futile. This applies to all cases, whether they be of the acute or chronic types. For a child this means treatment in bed, because in no other way can rest be insured. If the child is allowed to go about, little or no amelioration will take place, and the disease will drag on for months. No more striking testimony can be brought forward in favor of rest than the fact that a child with chorea may attend the out-patient department of a hospital for months without benefit, but,

if admitted to the hospital and treated in bed, in the course of ten days or a fortnight the condition will be relieved, and afterward, by the judicious control of the child's life, a permanent cure may be effected. It is practically useless to advise the mother of a hospital out-patient to give the child rest. The instructions are generally neglected, and the child is allowed to romp and play with his companions. The consequence is that the child may become excited, and this cannot fail to exercise a deleterious effect on the condition. In private practice the want of efficient rest will often delay convalescence for many weeks, although in other respects the circumstances are more favorable. It is extremely difficult to persuade the parents of a child who has chorea of a very mild type that rest in bed is essential, but it is only thus that a rapid cure can be effected. The quieting effect of rest in bed does much to allay the muscular irritability, and the freedom from excitement, which can best be insured by this means, helps to allay also the mental instability. There is only one circumstance which contra-indicates rest in bed. It sometimes happens that if a child with mild chorea be put to bed, he becomes very depressed, and this is bound to influence adversely the condition. In such cases, which are fortunately rare, forcible detention in bed will do more harm than good, and, therefore, one must needs be content with modified rest. The child with mild chorea does not feel ill, and so detention in bed suggests to his mind something of the nature of punishment. In such a case the child may be kept in bed for an hour or so each day, perhaps until noon, and then be allowed to get up and rest on a couch. The length of time a child must be kept in bed, of course, varies, and each case requires individual consideration and must be judged on its merits. In some very mild cases it may not be necessary to keep the child in bed for more than a few days, but afterward the child must rest on the couch for several hours each day, and violent exercise or excitement must be prohibited. Few cases require treatment in bed for longer than five or six weeks, and for an average case in which the symptoms are marked, but not acute, three weeks or a month will generally suffice. In all cases after the child gets up he must take things very easily, and no exertion, either physical or mental, should be permitted for some weeks. To allow a child who has been for a time in bed to indulge almost immediately in cycling, football, rowing, etc., will undo all the good work, and will very likely lead to a relapse. One has only to remember that chorea is most probably a complication or manifestation of rheumatism to understand why rest should be so persistently indicated. In chorea there is the possibility of cardiac involvement, and the severity of the attack is no criterion of the damage that may be done to the heart. Indeed, it is very often in the mild cases that most damage to the heart occurs. This fact is a very strong point in favor of the treatment of mild chorea by rest in bed, and afterward for enforcing the gradual return to healthy and vigor-

ous exercise. It is, however, unwise to keep the child too long in bed, and he should be permitted to get up at the earliest possible moment consistent with safety. Much harm is done by keeping the child in bed for weeks, and it would be better policy to treat him by modified rest on a couch, after say six weeks, although the choreic movements have not completely ceased.

**ISOLATION.** In cases of an acute or semi-acute nature, isolation is often required. In a hospital this may be conveniently carried out by having screens placed around the cot, or the case may be treated in a side ward. In the acute cases the child's limbs, especially at the knees and elbows, should be enveloped in cotton wool; the sides of the cot should be padded, and the mattress must be a soft one, or a water bed may be used, so that the patient may do himself no injury when tossing to and fro. In some cases a special nurse to attend to the patient is a matter of necessity. The child should certainly not be tied down in bed, a practice recommended by some. Such can only be described as heartless cruelty, and there is good reason to believe that choreic movements should be quite unrestrained. Any necessary restraint can be applied by the nurse, and a capable nurse can easily effect this purpose without the child being aware that he is being restrained. In private practice the question of isolation is a matter of much difficulty. The parents are, naturally, averse to the child being isolated, but they will generally consent if the matter be put before them in a proper manner. If the mother is a sensible woman, the child can be left in her charge, but the other members of the household should be excluded, or the child's nurse, if a capable person, may take him in hand. To leave a highly strung, nervous, and excitable child in the charge of a neurotic mother or nurse is useless, and the results of treatment will be disappointing. It requires a person of firmness and tact to undertake the successful charge of a choreic patient. While anything likely to irritate the child should be avoided, it is not advisable to pander to all his whims and caprices. If the mother or other members of the household are incapable (from a medical point of view) of looking after the child, then a trained nurse who is in sympathy with children should be engaged. It is often advisable to send the child away for treatment with a friend, or nurse, who is well known, and will be a congenial companion to him.

Bruehl<sup>1</sup> divides the rest and isolation treatment into four degrees of completeness, according to the severity of the case: (1) Going to bed early and rising late, so as to spend fourteen hours in bed; (2) going to bed also for two hours in the middle of the day; (3) absolute rest in bed for a fortnight, with very little visiting by relatives; and (4) darkening of the room, except at meal times. Except in bad cases it is not necessary to enforce strict isolation. In the milder cases, if it should be thought necessary that other members of the

<sup>1</sup> Rev. mens. des mal. de l'enf., June, 1906.

household should not see the child; it is much better to advise the sending of the child to the country, or to the seaside, along with some relative or friend.

**DIETING.** This is considered by many physicians to be an important desideratum in the treatment, and some enthusiasts have drawn up special dietaries. Dr. Goodhart believes in a special dietetic régime for these cases. He<sup>2</sup> recommends the following diet for chronic cases treated by massage, etc., and he says that in his hands it has proved of benefit.

"At 5.30 A.M., half a pint of warm milk and three slices of bread and butter (each slice an ounce in weight); 9.45 A.M., one-half ounce Kepler's malt extract in lemonade; 10 A.M., massage (fifteen minutes), followed by one-half pint of warm milk; 12.30 P.M., rice pudding, one-half pint of milk, green food, and potatoes; 4.15 P.M., one-half pint of warm milk, three slices of bread and butter, and an egg lightly boiled; 7 P.M., one-half ounce of Kepler's malt extract in lemonade; 7 or 8 P.M., massage, followed by one-half pint of milk. At the end of ten days or a fortnight the bread and butter is increased to four slices, a lean chop is added to the mid-day meal and an extra pint of milk is distributed over the twenty-four hours." For my part, with the exception of the acute cases, I make little alteration in the diet. In the acute cases I give a fluid diet consisting of milk, egg flip, beef tea, etc., but in the mild chronic cases I give an ordinary diet suitable to the age of the child, with an extra quantity of milk. The diet should be nutritious and easily digested, and will consist chiefly of bread, with butter or dripping, eggs, fish, chicken, rabbit, minced meat, milk, green vegetables, potatoes, and plain milk puddings. Sugar and starchy foods should be reduced to a minimum; indeed, it is well to forbid all sweet things. Tea, coffee, and alcohol should be avoided. It is important that considerable quantities of milk should be taken, but it unfortunately sometimes happens that the child will not tolerate large quantities, or may even refuse to take any milk. The milk may be modified in various ways, and may then be more acceptable to the patient. The milk may be diluted, either with ordinary water, lime water, or soda water. Mixing the milk with mucilaginous fluids, such as barley water, or thickening the milk with a little corn flour or gruel will render it more digestible. Perhaps the child will take the milk when peptonized, or will tolerate it when predigested, that is to say, in the form of "junket" or "curds and whey." Koumiss may be preferred by some. In the acute cases when the patient is on strictly fluid diet, it is a great loss if he cannot take milk or modified milk. There is nothing that equals milk as a nutrient fluid. It should be mentioned that in the very acute forms of the disease it may be necessary to administer nourishment in the form of nutrient enemata.

<sup>2</sup> Goodhart and Still's *Diseases of Children*, p. 807.

**THE BOWELS.** The bowels must be attended to, and every endeavor should be made to insure their regular action. An aperient is given occasionally if necessary. Some give a small dose of calomel now and again, but the actual aperient is not important, provided the bowels act regularly.

**EXTERNAL APPLICATIONS.** Many external applications have been recommended at one time or another, but some are worthless. The hot pack is employed by some practitioners, and certainly this undoubtedly exercises a beneficial effect in many instances and its application is often followed by sound and refreshing sleep. It is a form of treatment which has a peculiarly soothing effect on the patient, and more than anything else earns his gratitude. If the movements are not too violent a warm bath at night has a distinctly calming effect, and may overcome insomnia. In cases in which there is hyperpyrexia cold packs should be used, and during convalescence or in the mild forms cold or tepid sprays should be employed. The cold spray is invaluable: for the first few times it may be well to employ tepid water, but cold water should be used as soon as possible and will be found most invigorating. It is well to remember that the cold spray should only be continued if a healthy reaction follows its application, that is to say, when the patient is afterward rubbed with a towel there should be a warm glow of the skin, and he should feel warm, not cold. The application of blisters to the spine, the use of the ether spray to the spine, and the freezing of the spine with ethyl chloride are unnecessary and useless. Massage is of great value and should be carried out night and morning after the acuter symptoms have subsided. It is especially useful in cases in which there is any muscular wasting or any tendency to paralysis. This massage should be practised for ten to fifteen minutes, night and morning, and should only be carried out under skilled supervision. The massage is at first gentle rubbing, and is then succeeded by kneading of the muscles. The exponents of electrical treatment have not only failed to demonstrate its superiority over massage, but have also failed to prove its value.

**DRUGS.** The drugs that have been recommended for chorea are legion. That internal medication often renders important services can scarcely be denied, and the benefits derived are chiefly in the chronic cases. It is doubtless true that many cases would recover with simply rest, good food, and nursing, but I feel sure that the cure is hastened and convalescence shortened by certain drugs. Among the drugs that have been tried are: Zinc sulphate, arsenic, sodium salicylate, potassium bromide, ammonium bromide, veratrum viride, acetyl-salicylic acid, antipyrin, exalgine, trional, bromural, chloretone, strychnine (Trousseau), conium (Harley), ergot (Eustace Smith), etc. I have had experience with six of these drugs, namely, antipyrin, potassium bromide, sodium salicylate, chloretone, arsenic, and acetyl-salicylic acid. The first three I have found of



little use, and I have never been able to satisfy myself that they exercised any beneficial effect on the morbid process. Antipyrin and potassium bromide have never received much support except for their sedative properties, but salicylate of sodium has many advocates, among whom none is more enthusiastic than Dr. D. B. Lees, of London. He advises<sup>3</sup> enormous doses of the salicylate of sodium, 200 grains or more per diem, and he prescribes along with it large doses of bicarbonate of sodium. He is emphatic in his assertion of good results, and other observers have also spoken favorably of it. In my hands the drug has been an absolute failure, and other physicians have also had this experience. I do not give anything like the large doses recommended by Lees, as I consider the exhibition of these enormous quantities of this drug a very risky procedure. Chloretone I have used in only two cases (mild), and although recovery followed, it is doubtful whether the credit should be given to the drug. Wynter,<sup>4</sup> however, speaks of its value in several cases, but Ranking<sup>5</sup> records a case in which it was apparently worthless. Voelckner supports Wynter<sup>6</sup> in testifying to the value of this drug. He says: "The period of attack, the severity of the movements, and the mental instability were all favorably influenced by the drug, but it has some minor disadvantages, in this, that it is rather apt to make the children too drowsy, and there is sometimes produced an erythematous rash and the eyes get a puffy appearance not unlike that produced by whooping cough, but unaccompanied by albuminuria." With arsenic and acetyl-salicylic acid I have had good results, and the improvement was so marked after the exhibition of these drugs as to justify the conclusion that they played a part in the cure. With regard to arsenic, this was for many years the sheet anchor in the treatment of chorea, and certainly good results followed its use in a number of cases. Of late there has been a reaction against its employment, and this reaction is probably directly due to the haphazard method in which it was being prescribed. It was given by many simply because it had a reputation of being the drug to cure chorea, and no scientific reason was forthcoming. One great objection to it is that the condition is liable to recur as soon as it is discontinued. As regards the mode of administration, it is generally given as Fowler's solution, and the dose is small to begin with, and is increased gradually until large doses are being taken. My practice was to prescribe 3 to 5 minims of liquor arsenicalis three times a day, and increase the dose by 2 minims every second day until the child was taking 16 to 20 minims of the liquor Fowleri thrice daily. By the time this dosage had been reached the movements had ceased, and then the doses were gradually decreased in the same ratio as they had

<sup>3</sup> The Treatment of some Acute Visceral Inflammations, and other papers, London, 1904.

<sup>4</sup> Lancet, London, March 30, 1907.

<sup>5</sup> The Hospital, January 11, 1908.

<sup>6</sup> Folia Ther., April, 1908.

been increased; and the child continued to take 5 minims of liquor arsenicalis thrice daily for some weeks. By this means many cases recovered. Small doses of arsenic are useless, and the opinion of most of those who have used arsenic successfully is that large doses, which are worked up to gradually, are necessary. The arsenic should not be abruptly stopped. It is true that occasionally symptoms of poisoning supervene. I have had one such case in which a little girl, aged seven years, when taking 12 minims of the liquor arsenicalis, developed toxic symptoms, indicated by peripheral neuritis and a punctate erythematous rash. On withholding the drug for forty-eight hours the symptoms disappeared, and the drug was then continued, but in more moderate doses. Gordon Sharp<sup>7</sup> believes in saturating the tissues rapidly with arsenic. For a child between eight and fifteen years of age he orders:

R—Liq. arsenicalis. . . . .	℥ss
Tinct. capsici . . . . .	℥xxv
Ext. glycyrrhizæ liq. . . . .	℥ss
Aq. chloroformi . . . . .	℥vj
Aquæ . . . . .	ad ℥xij
M. Sig.—One tablespoonful three times a day immediately after meals.	

That means that the child at once takes 10 minims of Fowler's solution in each dose, and this is 2 minims more than the maximum dose of the British Pharmacopœia. If after a week no improvement is manifest, he increases the amount of the liquor arsenicalis in the mixture to 300 minims. He believes that if arsenic is going to do good in chorea, it will show its beneficial action within the first fortnight. When progress is being made he continues this treatment until the patient can walk along a straight line, or stand on the leg of the affected side with steadiness. After all the movements have ceased he prescribes the following:

R—Sodii bicarb. . . . .	℥ij
Tinct. capsici . . . . .	℥xxv
Ext. glycyrrhizæ liq. . . . .	℥j
Aq. chloroformi . . . . .	℥vj
Aquæ . . . . .	ad ℥xij
M. Sig.—One tablespoonful three times a day after meals.	

According to him this latter mixture is given because it "washes the arsenic out of the tissues;" but he admits that the statement may not be scientific.

Objection has been taken to arsenic in certain quarters. Burnet,<sup>8</sup> in discussing the treatment, vigorously attacks arsenic as a remedy for this disease. He sums up his objections to it as follows: (1) Large doses have to be given, and these may induce neuritis; (2) the results achieved are rarely permanent; (3) arsenic exercises no

<sup>7</sup> Practitioner, February, 1908.

<sup>8</sup> British Journal of Child. Dis., October, 1908.

influence over the complications and sequels of chorea; and (4) it does not benefit in any way the rheumatic constitution of the patient. He believes that the cure by arsenic is brought about by poisoning and probably paralyzing the nervous system. Koplik<sup>9</sup> attacks arsenic on the ground that it is dangerous because of its effects on the kidneys. When arsenic is given by the intensification method, albumin may appear in the urine before any other toxic symptoms, sometimes when only fifteen drops of the liquor are being given daily to a child aged six or eight years; this clears up when the treatment is suspended. Casts may also appear, and even blood cells. Koplik states that the urine is the best test for the limit of toleration of arsenic. I have never found albuminuria after the administration of large doses of arsenic in any of my cases, not even in the one in which toxic symptoms resulted. Still it is a danger that *must be kept in mind*. Though arsenic will bring about recovery in many instances, it must be admitted that Burnet's contentions are most reasonable, and one is, therefore, inclined to discontinue this drug as an active agent in the treatment of chorea if a better drug can be found.

During the last three or four years I have relied on acetyl-salicylic acid, and I have come to regard it as the drug *par excellence* for the treatment of chorea. I have placed on record some of my cases<sup>10</sup> which were treated with this drug, and since then I have used the drug in practically all my cases, and up to the present it has not failed to effect a cure. Wall<sup>11</sup> speaks highly of the drug, and Burnet<sup>12</sup> has had very favorable results in his practice. This drug was originally introduced as an antirheumatic remedy, but its usefulness is not limited to those cases of chorea in which there is a history of rheumatism. It does well in all cases, whether acute, subacute, or chronic. After salicylate of sodium has failed to effect a cure, acetyl-salicylic acid may prove of benefit, as is indicated by the following case:

I. R., a girl, aged eight years, came under observation in March, 1907, for chorea. It was her first attack, and characteristic choreiform movements of fairly acute nature were manifest. There was a strong rheumatic history. She was put on sodium salicylate (20 grains every six hours), but after three weeks of this treatment no appreciable benefit had resulted. Acetyl-salicylic acid (10 grains every four hours) was then substituted; immediately a change for the better was noted, and in a fortnight the patient was cured of her attack. In this case the salicylate was given a fair trial, but apparently exercised no curative effect on the disease. One would have thought that in a case in which there had been rheu-

<sup>9</sup> Medical Record, January 18, 1908.

<sup>10</sup> The Hospital, July 27, 1907.

<sup>11</sup> Therapeutical Society's Transactions, 1907; also Medical Press, May 20, 1908.

<sup>12</sup> Loc cit.

matism the salicylate would have acted well, but it only confirms the observation of others, who have noted that chorea may develop in a patient suffering from rheumatic fever and under treatment with salicylates, which evidently therefore have no prophylactic effect on the condition. In non-rheumatic cases acetyl-salicylic acid doubtless acts in virtue of its analgesic and sedative properties; for children it is far superior to sodium salicylate, because its taste is not unpleasant and because ill effects are less likely to follow its use. The sweet, mawkish taste of sodium salicylate (and a more disgusting taste can hardly be imagined) cannot be covered, and in many cases the forcing of the child to take this drug would probably do more harm than good. Acetyl-salicylic acid may be given in powders, in cachets, or in a mixture. My experience is that the last is the best method for children, and the following prescription will be found useful:

R.—Acid. acetyl-salicylic . . . . .	5iiss
Gum acac. . . . .	q. s.
Syr. aurantii . . . . .	3j
Aq. chloroform . . . . .	ad 3iv
M. Sig.—A dessertspoonful every four hours.	

This is suitable for a child aged six years. The dose is increased to suit the age of the child, and for children at or about puberty 90 to 120 grains may be given in a day. It should never be given in tabloid form, and it should not be prescribed with alkalis. As regards unpleasant symptoms, these occasionally supervene after the exhibition of the drug, but far less frequently than with salicylate of sodium. In some cases gastric pain, vomiting, and giddiness follow. Tinnitus aurium is seldom met with. Painful œdema of the eyelid and lip has occasionally occurred. Epistaxis and erythematous eruptions are rare sequels. Lees<sup>13</sup> has recorded a case in which coma was produced. I have not had any such symptoms in cases of chorea in children in which this drug was used. The only symptoms that I have noted after the use of acetyl-salicylic acid (in conditions other than chorea) have been excessive perspiration in a few cases and tinnitus aurium in one case. It is not improbable that the bad effects may be attributed to faulty methods of prescribing or dispensing the drug. Gastric symptoms may be avoided if the precaution is taken of giving the drug only after meals and never on an empty stomach. The drug is not so likely to depress the heart as salicylate of sodium, although there are some who maintain that physiologically pure salicylate of sodium, if properly given, will not act as a cardiac depressant.

Since employing this drug in chorea I have never had to use hypnotics to induce sleep, even in acute cases. The following case, seen in March, 1908, may be quoted in illustration:

<sup>13</sup> Loc cit.

Annie G., aged sixteen years, came under treatment for acute chorea, the complaint having started three days before. No history of rheumatism. The movements were very violent, and she had to be constantly watched to prevent her doing injury to herself or throwing herself out of bed. She was quite unable to feed herself, and had no control over the sphincters. She was given fluid diet, and acetyl-salicylic acid (20 grains every four hours) was prescribed. During the first night she only slept for a couple of hours, but afterward she slept well. In a week's time all the movements had ceased, and after another week's rest in bed (with gradually decreasing doses of the acetyl-salicylic acid) she was able to get up and go about. It is doubtful whether simply rest in bed and dieting would have brought about this rapid cure. The behavior of this case would seem to lend support to the contentions of some German authorities, who maintain that acetyl-salicylic acid has an hyponotic as well as an analgesic effect. It should be noted that the drug should not be discontinued immediately on the cessation of the movements, but should be gradually stopped, and it is frequently advisable to continue giving it in small doses for many weeks. There need be no fear in advising the drug, because there is no tendency to sweating in a person going about if it be taken in moderate doses (5 grains twice or thrice daily). From the above facts it must be concluded that in acetyl-salicylic acid we have a most useful drug. Pleasant to take, comparatively free from unpleasant symptoms, and reliable in its results, the drug is one which should command attention and is well worthy of a premier place in the medical man's therapeutic armamentarium. The use of the drug is also based on scientific grounds, because it is antirheumatic and because its properties are analgesic and sedative, and, according to some, are also hypnotic.

With other drugs I shall only deal briefly. One or two have been so highly recommended by eminent physicians as to merit brief consideration. Of such drugs, trional may be mentioned. Voelcker believes that in trional we possess a drug which has a distinctly beneficial effect in chorea, both in alleviating the symptoms and in reducing the time required for the treatment of the disease. It does not cause cardiac depression, and the only unfavorable condition noted by him has been the very occasional occurrence of rather vivid dreams. He gives 5 grains three times a day as an initial dose to a child over four years, but the dose is gradually increased until the child is taking 5 grains every six or every four hours. He believes it is more advantageous to administer smaller doses at shorter intervals than to give larger doses at longer intervals. The following mode of exhibiting trional has been suggested:

R <sub>x</sub> —Trional . . . . .	gr. xv
Pulv. sacc. alb. . . . .	5ij
Gum trag. . . . .	gr. iij
Gum. arab. . . . .	gr. iij
Aq. flor. aurant. . . . .	5iiss
Aq. laur. ceras. . . . .	5ss
Misce et fiat emuls.	

Sig.—One-third part to be taken in milk or water as a single dose.

Strychnine has found favor with some. Trousseau was a most enthusiastic advocate of strychnine, and Ewart<sup>14</sup> has recently written about it. It will probably be more especially useful in cases in which there is muscular wasting or in paralytic cases. The more hypnotic drugs, such as chloral, chloralamide, etc., are also used, but while it may be necessary to give such drugs occasionally in order to permit of the patient's getting sleep, it seems to me that they should not be used as part of the routine of treatment.

The fact that chorea may be a manifestation of rheumatism must be borne in mind, and the heart should be frequently examined to see that there is no cardiac involvement. It is probable that the value of strychnine rests in its acting as a cardiac tonic. In some instances there is serious damage to the heart, and it becomes imperative to deal efficiently with this. Strophanthus may be given, digitalis in my opinion not being a suitable drug for children. The following combination is a good one:

R <sub>x</sub> —Tinct. strophanth. . . . .	5j
Liq. strych. hydrochlor. . . . .	5ss
Spt. aeth. . . . .	5ij
Syr. aurant. . . . .	3j
Aq. chloroformi . . . . .	ad 5vj

M. Sig.—One tablespoonful three or four times daily for a child of five.

During convalescence tonic treatment is advantageous and is often required, because there may be considerable anemia. Iron in one of its various forms may be given, or iron may be combined with arsenic or cod-liver oil. A mixture of compound syrup of ferrous phosphate and cod-liver oil is well taken by children. My own experience recently is that small doses of arsenic form a valuable therapeutic agent for overcoming the condition of anemia. After the movements have ceased under treatment with acetyl-salicylic acid, and when this drug is being given in 5-grain doses two or three times a day, it has been my custom to prescribe 3 or 4 minims of the liquor arsenici hydrochloridi thrice daily, and, in several of my chronic cases with anemia, with very gratifying results. Any reflex irritation, as, for example, phimosi, carious teeth, worms, etc, while not, perhaps, an actual cause of chorea, will certainly aggravate the condition, and therefore they should be remedied.

<sup>14</sup> Trans. Soc., Study of Diseases of Children, 1906, vi, 192-95.

AFTER-CARE. A child has been treated and has recovered from the attack, but our efforts are not yet ended. Unless the child's life is carefully regulated, a relapse may take place. The child must on no account be permitted at once to indulge in physical or mental exertion. Quiet games which do not involve excitement may be allowed, but anything of the nature of racing should be prohibited. Return to school must not be thought of for two or three months, and then the lessons should be carefully regulated, and the child should not be driven to work. Some of these children are intellectually brilliant, and competitive examinations should be forbidden, or, at any rate, discouraged for such children. The excitement or strain of these examinations may be quite sufficient to determine an attack of chorea. On the slightest evidence of the return of the malady the child should be taken from school and sent into the country, away from its present surroundings. Inattention and fidgetiness are frequently seen in early cases, and a child is often unjustly punished on account of these symptoms. Again, the child may be afraid to sleep in the dark. In such circumstances the child may have a light in the bedroom at night, or an adult may sleep in the room with the child. A child who is threatened with chorea should not be constantly corrected or whipped. By judicious sympathy an attack of chorea may be averted. But a certain amount of firmness is necessary if one does not wish the child to grow up a pampered little pet. The services of a person of discretion who can tactfully and with judgment exercise this firmness are of inestimable value for such a child.

To sum up: Rest is the *sine qua non* of treatment in every case of chorea. In the more acute cases isolation is required, but in the mild cases this is unnecessary and may even be harmful. For the average case a liberal, easily digested diet is the best, and hydrotherapy may be useful. Massage, judiciously employed, is of undoubted value. Of drugs, acetyl-salicylic acid is the most reliable. It can be recommended on scientific grounds and because practical experience has proved its utility. In some cases tonic treatment is required, and arsenic in small doses is especially valuable. After recovery the child requires careful supervision, and the child's life must be very carefully regulated. On any indication of the return of the malady prompt measures must be enforced to check the attack.

Such, then, are some of the points in the treatment of chorea, a disease which, although not often fatal, is the cause of much annoyance to parents, and results in considerable suffering (largely mental) to the child.

## THE THERAPEUTIC USE OF PASSIVE HYPEREMIA (BIER).

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INTRODUCTION. The present conception of inflammatory processes is, that as a result of injury—mechanical, thermal, bacterial—the tissues react locally, and exhibit certain phenomena which always have a distinctive tendency to produce repair of the damaged tissue. The old teaching, that inflammation is harmful and to be combated by every means at our command, has given place to the idea that reaction is necessary after injury, and if it does not occur measures should be taken to promote and increase it. In recent years we have had several important advances in treatment along these lines, and while the principles upon which they are based have been evolved by many workers, yet to Bier,<sup>1</sup> von Mikulicz, and Wright<sup>2</sup> we are indebted for passive hyperemia, methods of increasing the “resistance period,” and opsonic therapy.

As a result of irritation to some more or less limited area of the body the phenomena of inflammation appear in a fairly well-regulated manner, and unless overcome by the greater power of the irritant, they inaugurate the sequence of events which we speak of as repair. The transudation of fluid from the vessels into the tissues, the emigration of leukocytes, the formation of new blood paths, and the stimulation and proliferation of the fixed connective-tissue cells are well known as part of the process of repair, and yet most of us are prone to forget that these very processes are not only capable of producing new tissue, but that they are also potent agencies in the removal of the irritant. By noting this fact, we are led to the conclusion that hyperemia and inflammation, up to a certain degree, are beneficial and should be artificially encouraged if the irritant itself does not stimulate nature to produce a degree of hyperemia sufficient to subdue the disease. At first thought the intense swelling, pain, local heat, and redness inseparable from acute inflammation would seem to indicate that the area of infection is suffering from an excessive reaction. But, as Adami<sup>3</sup> remarks: “The majority of cases of acute inflammation, cases which from their symptoms call for interference, are truly examples of inadequate reaction; the forces which the organism has been able to oppose to the irritant have been insufficient to neutralize it.”

Before discussing the rationale of Bier's passive congestion, it might be well to consider the reactive processes generally. I know no better scheme than that of Adami into which they may be divided: (1) Reaction inadequate to neutralize the irritant and bring about

<sup>1</sup> Hyperämie als Heilmittel, Leipzig, 1907.<sup>2</sup> Jour. Amer. Med. Assoc., 1907, xlix, 479, 567.<sup>3</sup> Inflammation, New York, 1906.



repair; (2) reaction adequate for these purposes; and (3) excessive reaction. In the natural repair of fractures, the healing of incised wounds, etc., when the irritation is of mild grade and unaccompanied by severe signs or by pus formation the local reaction is adequate, and repair depends upon the healthy condition of the blood and, to a certain extent, of the nervous system. These are dependent, of course, upon a healthy coördination of all the component parts of the organism, as a whole, and the surgeon simply has to bring the wound or injury into such a condition by aseptic methods, etc., that an adequate local reaction is attained, and by regulating the excretory organs such reaction is preserved. No further treatment is necessary.

If the reaction is inadequate the surgeon should not attempt to lessen the inflammatory manifestations, but, on the contrary, they should be promoted and even increased in the hope of destroying the irritant locally. As has been remarked already, the symptoms of inflammation may be pronounced and an excessive reaction diagnosed, but the spreading character or progressiveness of the infection and the general bodily reaction will easily show that the forces of nature are insufficient to cope with the irritant. This class is the one in which Bier's artificial hyperemia finds its use, and Wright's bacterins can be applied with most hope of success.

Excessive reaction is met, according to Adami, in only two conditions: (1) When one or other factor in the process is unduly exalted, the others being unduly low; and (2) in certain cases of what we may term neurotic and referred inflammation. Necrosis, ulceration, adhesions, or cicatrices are not examples of this class, because they simply mean "that the virus is being antagonized at great cost." Virulent infections and low resistance causing paralytic dilatation of the vessels without leukocytic emigration, exuberant granulations, keloids, the swelling about a sprain of the ankle, etc., are examples in which the hyperemia requires to be lessened, not increased. With these facts in mind we are better able to take up the method whereby Bier induces hyperemia (*Stauungshyperämie*), of which Murphy remarks that there is nothing that has come into surgery in the last ten years as a practical application that appears to him to have as much value.

Of course, the idea is not new, as the production of congestion by cupping, by heat, and by counterirritation was done by the ancients, and, as Bier points out, Paré used the constricting bandage to produce callus formation in badly uniting fractures. Bruns, in 1886, reported five cases treated by congestion, Thomas, in 1886, used the method in 14 cases, and referred to it as "damming," and Helferich, in 1887, again recommended congestion as a stimulus to bone formation. Before these times, however, certain clinicians had stated that pulmonary tuberculosis and pulmonary stenosis often coincided, due to the anemia of the lung, and Rokitansky enunciated the theory that mitral stenosis, with its chronic passive congestion of the lungs,

would prevent the development of tuberculosis. The latter statement has since been severely attacked, but they both came to Bier's notice and he proceeded at once (1892) to produce hyperemia in an effort to influence the course of tuberculous arthritis. Encouraged by the results obtained in the treatment of surgical tuberculosis, he enlarged the scope of his method, and applied it to acute and suppurating processes of all kinds. In 1905 Klapp,<sup>4</sup> from Bier's clinic, introduced the use of the various suction apparatus.

It is, of course, clear that we can increase the blood in a given area in two ways: (1) By producing a more active flow of arterial blood by accelerating the local circulation by the application of heat, counterirritants, etc. This is called active hyperemia and has been highly developed by Bier, being especially adapted to the treatment of chronic cases. (2) By obstructing the venous return, the blood is dammed back upon the capillaries, dilating them, and thus increasing the amount of blood (passive hyperemia). The suction apparatus produces both kinds of hyperemia, although Bier and Klapp believe the passive form to predominate. Even in the active form the dilatation of the bloodvessels causes slowing of the current, but as Bier teaches, both the arterial and venous hyperemia act so nearly alike as to make discussion on this point of little moment. Another fact has recently been brought to our attention by Bier, Schede, and others: that is, the fallacy of the old idea that by the use of cups, heat, iodine, blisters, etc., superficial congestion produces a deep anemia. This is often spoken of as "depletion of the part affected," and while this may occur to some degree in very mild forms of counter-irritation, in most cases hyperemia is probably produced.

**METHODS OF APPLICATION.** *Active Hyperemia.* Hot air has been used to produce hyperemia as long as the healing art has existed, and every one is familiar with the use of hot baths, hot fomentations, sun baths, steam baths, and the like. This method is particularly applicable to those chronic conditions in which thickenings, infiltrations, exudates, or adhesions exist, the result of a previous acute inflammation, as their absorption is much aided by flushing the parts with healthy blood. In certain neuralgias and other pains it is often of remarkable, although of uncertain benefit. Most of us are familiar with the well-known baking apparatus, and have used it with more or less success, depending upon the nature of the condition subjected to the heat. Bier has only simplified the method and narrowed its field of usefulness, thereby increasing the probability of successful treatment by its means. He recommends simple, inexpensive boxes made of wood free from resin, covered with cloth, and having the inner surface soaked in silicate to prevent burning. Openings are provided for the limbs, for a thermometer, and for the pipe from the apparatus generating the heat, which is simply a long sheet-iron

<sup>4</sup> Münch. med. Woch., 1905, No. 16.

funnel, under which an alcohol, gas, or electric lamp is placed. If gas is used, the lamp should always be lighted before placing it under the funnel. The lid should contain several holes to permit the escape of air, thus insuring dryness. Different-sized boxes, with differently placed openings are used for the various joints, although some degree of combination is possible.

The limb is placed in the box, the lamp lighted and placed under the funnel, and the temperature gradually raised to a point which is comfortable to the patient. This may be 150° F., or it may be even as high as 250° F. It should be borne in mind, however, that with increased heat the part becomes less and less sensitive, and at 250° to 300° F., sensation is almost nil, so that burns may occur. After one-half to one hour of treatment the lamp is turned off, and fifteen minutes later the limb may be removed from the box. The length of treatment and whether it be given daily or not depends upon the reaction.

*Passive Hyperemia.* No adequate English word has yet been devised as the equivalent of *Stauungshyperämie*, the usual designations used being passive, congestive, induced, or obstructive hyperemia. Allen and Meyer believe that the German word should be taken over bodily into our language, but as most of the articles upon the subject are classified in the indexes as passive hyperemia, I have preferred in this article to use that term. When the condition to be treated involves the head, extremities, scrotum, or testicles, the hyperemia is produced by means of an elastic bandage. When this is not feasible, as upon the back, chest, pelvis, and surface of the body generally, various forms of suction apparatus are used.

The elastic bandage used by Bier is made of soft rubber, 2½ inches wide and sufficiently long to be wrapped six or eight times around the limb, and then fastened by a safety pin, tapes, etc. The method he adopts is about as follows: If the condition to be treated is, for example, an infection of the foot, the bandage would be wound about the thigh, each time overlapping slightly. The bandage is put on sufficiently tight to hinder definitely the venous return, but not sufficiently so as to diminish the arterial flow, the latter point being determined by feeling the pulse below the obstruction. In a few minutes the limb begins to swell and becomes of a deep red color up to the bandage, the skin feeling warm to the touch. When the swelling is well established serum begins to escape freely from any wound which may be present. A little later the limb appears bluish or bluish red, but it should never be white or blotchy.

The swelling or oedema is always present if the bandage is continued for several hours, and need occasion no alarm if the pulse is felt below, the limb is warm, and pain is absent. This oedema, however, should not be allowed to persist, but between applications absorption should be promoted by elevating the limb and by massage. The bandage remains in situ for from one to twenty-two hours,

depending upon the condition for which treatment is instituted, but its position should be changed after about ten hours in one place. When long applications are used the skin may be protected by a soft flannel bandage beneath the rubber. The bandage must always be placed upon a healthy portion of the limb. When the patient's tissues are very sensitive, an inflatable tube may be used, similar to the arm band of the Stanton sphygmomanometer. Such a bandage has been described by Henle<sup>5</sup> and more recently by Wilson<sup>6</sup> and Grace.<sup>7</sup> The use of webbing instead of rubber has also been suggested.

Bier insists upon the utmost care and watchfulness, especially in the first day or two. The physician himself should attend to the treatment, as the method is capable in acute cases of doing almost as much harm if improperly applied, as it does good if correctly done. The progress of the case is gauged by the local appearances and symptoms—disappearance of pain, improvement in pulse, lowering of temperature, and finally the less and less response of œdema to the bandage. In the interval there may be a rise in temperature due to the setting free of toxins, and in septicemia the action upon the temperature may for some time be inappreciable.

The following must be rigidly avoided to insure success: Pain, paresthesia, white œdema, coldness of the skin, and obstruction of the arterial blood supply. All dressings and bandages must be removed the wound being protected by a loosely applied sterile towel; severe cases should be treated in bed; all pus should be evacuated by as many incisions as may be necessary, but these need not be as long as when passive hyperemia is not used, nor should the wound be packed or curetted; free incisions are only required when the circulation of the part is seriously impaired.<sup>8</sup>

*Suction Apparatus.* Although cupping has been practised since time immemorial to "relieve inflammation" and has been used in a more or less crude manner for years in the treatment of ulcers and infections, yet the method was not upon a scientific footing until Klapp, with the aid of an instrument maker, perfected the various shaped cups now on the market, and showed how they could be used with astounding success. These cups are devised to fit any part of the body, a furuncle on the neck, an abscess on the buttock, or a fistula at the knee-joint, for instance. The cup simply consists of a glass bell, with a heavy and usually curved rim to fit on a curved surface and a bulb attachment to exhaust the air. There are two essentials to be grasped before applying this method of treatment: (1) The diameter of the cup must exceed the area of infiltration; and (2) the amount of pressure must be regulated, because if the vacuum is too little, nothing is attained, and if too great, pain and white œdema are produced.

<sup>5</sup> *Zentralb. f. Chir.*, 1904, No. 13.

<sup>7</sup> *New York Med. Jour.*, July 4, 1908.

<sup>6</sup> *Jour. Amer. Med. Assoc.*, 1908, 1, 1122.

<sup>8</sup> See remarks under Excessive Reaction.

The rim of the cup selected is greased with vaseline, and the bulb compressed in the right hand; the cup is then applied over the furuncle or sinus, and the pressure slowly released. The skin and underlying tissues are sucked into the cup; the hyperemia appears as a red or bluish coloration; pus, serum, and blood ooze from the wound. At the end of five minutes the cup is gently removed, the exudate wiped off, and the part allowed to rest for three minutes, whereupon the cup is again applied. This intermittent treatment is continued for forty or forty-five minutes, and then a simple dressing applied. After the united suction a limpid serum is constantly exuded, sometimes containing blood corpuscles and bacteria, in amounts reaching from 5 to 8 c.c. Treatment is continued every day, gradually decreasing the time of application as the discharge becomes thinner and the granulations become red and firm. Sometimes a scab or crust forms over the sinus which requires removal before beginning treatment. I find the use of Wright's sodium citrate chloride solution very advantageous in preventing clogging of the sinus with thick exudate. Squeezing, probing, curetting, or the use of drains is absolutely contra-indicated. Unless seen in the early stage, furuncles, carbuncles, suppurating lymph nodes, or abscesses should be opened by a small incision, and the cup applied immediately. Cold abscesses may safely be opened if due care is exercised in their protection, but should not be curetted, probed, or injected with iodoform emulsion; nor is immobilization necessary. Very large suction glasses are made for the treatment of puerperal mastitis, and are provided with a suction pump and stopcock arrangement. Finally, large and rather expensive glass vessels are made, into which a whole limb may be placed and suction applied. With the exception of a small one to fit the finger in the treatment of felons, they can be superseded by the elastic bandage. They can easily be made for the hand and wrist, however, by fitting a rubber sleeve to the opening of a large glass irrigator and a tube and stopcock to the outlet pipe. A Martin rubber bandage wound around the cuff makes it fit air-tight around the arm. A bicycle pump is used to produce the vacuum. Their best use is seen in orthopedic practice, as stiff joints may be gradually mobilized in a nearly painless manner.

**MODE OF ACTION.** Bier does not ascribe the beneficial action of passive hyperemia to any one factor, and, owing to the complexity of theories regarding the protective process of the body against infection or toxemia, it is difficult to explain clearly, by scientific reasoning, how this method exactly acts. Bier, in his early publications, offered no explanation, except the flushing effect of the saturation of the tissues with serum, and compared the process to an irrigation system, in which the outflow is interfered with and the soil inundated to an overflow. In later communications he states his belief that the bacteria and their toxins are rendered harmless and further necrosis of tissues prevented by the superabundant nourishment. Much experi-

mentation has led to some elucidation of the problem. Bier groups the beneficial effects under the following headings:

1. *Relief of Pain.* This is particularly emphasized by Bier, and serves as the main criterion by which the progress of the case is recorded. The pressure of exudate is not now considered as the cause of continued pain, but this is thought to be due also to the irritation of the sensory nerve endings by toxins. Ritter<sup>9</sup> believes that hyperemia reduces the sensibility of tissues by diluting the toxins, and also by correcting the isotonic difference between the products of inflammation and the tissues in which they lie. The pain usually recurs in the intervals of treatment, at any rate, for the first few days, and in spite of the most careful application of the method I have several times in bone lesions produced an increase of pain by the constricting bandage.

2. *Bactericidal Action of the Serum.* The experimental proof which Bier offers in support of the action of the oedema upon the bacteria in the affected tissues is mostly based upon the findings of Nötzel,<sup>10</sup> in 1899. This experimenter injected fatal doses of anthrax and virulent streptococci into the tissues of 67 rabbits in which passive hyperemia had been produced. Fifty-one lived and 16 died, the latter, however, all had the "white oedema," which is to be strictly guarded against in producing the congestion. The control rabbits all died. Joseph,<sup>11</sup> Colley,<sup>12</sup> Hambürger,<sup>13</sup> and Lacquer<sup>14</sup> believe that the oedematous lymph, produced during periods of congestion, is markedly bactericidal. Baumgarten<sup>15</sup> agrees with Nötzel's findings if the dose of anthrax bacilli is not large, but he obtained negative results after injecting tubercle bacilli. While believing that there is a certain bactericidal action on the part of the accumulated blood serum, he suggests that this is not vigorous and that the death of bacteria may be due to the lack of nourishment in the media. This seems to me to be based on false premises, in view of the well-known predisposition of chronic oedema to bacterial invasion.

On the other hand, many experimenters have failed to obtain this bactericidal action, among the more recent being Wrede,<sup>16</sup> Franzenheim,<sup>17</sup> Graff,<sup>18</sup> and Walther.<sup>19</sup> Wrede, in particular, believes that the bactericidal power is uncertain and can be used only in a limited way, and in 50 cases he repeatedly examined the incised focus and was unable to demonstrate by enumeration a marked decrease in the organisms. He also examined unopened foci, joints, for

<sup>9</sup> Arch. f. klin. Chir., Band lxxviii, S. 429.

<sup>10</sup> Arch. f. klin. Chir., Band lx, Heft 1

<sup>11</sup> Münch. med. Woch., 1906, No. 48, S. 2370.

<sup>12</sup> Ibid., 1906, No. 6.

<sup>13</sup> Virchow's Arch., 1899, Band clvi, S. 329.

<sup>14</sup> Zeit. f. Exper. Path. and Therap., 1905, Band x.

<sup>15</sup> Münch. med. Woch., 1906, Band iii, No. 48.

<sup>16</sup> Surg., Gynec., and Obstet., 1908, vii, 288.

<sup>17</sup> Arch. f. klin. Chir., 1908, Band lxxxvii, Heft 2.

<sup>18</sup> Beitr. z. klin. Chir., 1908, Band lix, Heft 3.

<sup>19</sup> Virchow's Archiv, 1908, Band xciv, Heft 1.

instance, which had been treated for some time by passive hyperemia, and found many actively growing bacteria.

Without going into the controversy in detail, it may suffice to point out that in all probability the success of this method of treatment depends upon the coincident working of increased serum, bacteriolysis, and phagocytosis. By increasing the pressure in the capillaries the focus of infection is flooded by a lymph having antitryptic and opsonic powers, arresting the further destructive action of ferments and inhibiting bacterial growth. When the bandage is removed the dammed circulation reestablishes itself; the lymph moves out of the affected part, liberating more or less endotoxin, which exerts an influence upon the antibactericidal power of the blood generally by the stimulation of antitoxins, alexins, opsonins, etc. If any of the factors of this relation are altered the results of the method must vary. Thus, the period of the so-called "positive phase" is the most favorable for the success of Bier's method, as the blood serum comes to the focus of infection charged with bactericidal and bacteriolytic properties, and the leukocytes and opsonins are powerfully phagocytic. If the organism, on the other hand, is depressed and in the so-called "negative phase," passive hyperemia may fail in its purpose, or, what is more important, the liberation of the endotoxins in excessive amount, during the pause, may seriously affect the condition of the patient. For these reasons I believe that we will shortly have to modify the extravagant and universal claims of success for this treatment, and so balance the surgical incision, the artificial use of opsonins, and the increased lymph flow by passive hyperemia that they will each have their applications singly or together. At any rate, it seems as though, just as asepsis has succeeded antiseptics in operative technique, so will a more rational treatment of acute and chronic suppuration based on modern scientific principles succeed the douching of wounds with chemicals and their irritation by the continuous presence of foreign substances. It is well known that a film of necrosis results from the use of strong chemicals injuring the histological elements, and it should be equally well understood, as stated by Wright, "that the antiseptic will directly antagonize the protective forces which the living organism has at command, will paralyze the phagocytes, and will abolish the antibacterial power of the body fluids."

The papers published by Lexer<sup>20</sup> and by Wolff-Eisner,<sup>21</sup> in 1906, are very suggestive and emphasize the importance of recognizing the danger of the toxins produced by the bacteriolysis in severe cases. During the interval or pause in the treatment the œdema disappears and "the body is flooded by the œdema fluid which carries with it the soluble substance of the inflammatory process" (Wrede). This is often evident clinically by the rise in temperature and some-

<sup>20</sup> Münch. med. Woch., Band liii, No. 14.

<sup>21</sup> Ibid., Band liii, No. 23.

times by chills, etc. Lexer, therefore, points out that this injurious action may be avoided in severe acute cases, by large and early incisions in place of the small ones recommended by Bier. Such treatment also prevents the spreading of the endotoxins into hitherto intact areas. Wolff-Eisner states that the indications for Bier's hyperemia are the same as for the bactericidal serums, the hyperemia being most favorable when complete bacteriolysis is present, and the number of bacteria small. This is seen in mild cases and in severe cases treated early. He also observed that sometimes in streptococcal infection, either pure or mixed with staphylococci, the Bier treatment failed or actually caused a general exacerbation.

3. *The Resorption of Toxic Products.* Bier advances many ideas from physiological experiments to support this effect of hyperemia, of course basing his contention upon the well-known increase of lymph flow as the result of venous obstruction. Thus, Joseph measured the amount of oedema by the displacement seen when the limb is placed in a cylinder of water before and after the constriction. In one experiment he found that 450 c.c. of fluid passed out of the arm. If we are able to eliminate the effect of the liberated toxins upon the organism, these results would be ideal for all cases, but, as remarked before, the endotoxins must, if excessive, be reckoned with.

4. *The Softening and Solution of Blood Coagula and Exudate.* Bier states that adhesions, cicatrices, and contractions about joints become soluble under the influence of enzymes in the lymph with which they are flooded, and then absorbed. The flooding of unhealthy tissue during the intermittent oedema is followed by its absorption in the intervals and its replacement by a large amount of new healthy tissue. It is probable, also, that the increased number of phagocytes is a very important factor in favoring absorption.

5. *Increased Nutrition.* But little need be said on this point, as it has been believed since Virchow that hyperemia increases nutrition. The zone of reaction and cell growth usually seen about a focus of necrosis is evidence that the cells are actively assimilating. Care must be exercised not to prolong the hyperemia unduly nor to allow a condition of chronic oedema to occur, in which events the vitality of the tissues will be lessened, and the process become generalized.

CLINICAL APPLICATION. To attempt even a brief description of the various diseases for which hyperemia, active and passive, has been recommended would far transgress the limits of this paper. It suffices to state that from meningitis to gout and back again the list includes nearly every infection or nutritional disorder to which the body is heir.<sup>22</sup> The following are selected as types of the more

<sup>22</sup> For a full description of these the reader is referred to Bier's *Hyperämie als Heilmittel*, where over 200 pages are devoted to a discussion of the clinical uses of hyperemia.



common conditions to which the method is applicable. In general, it may be stated, "that for conditions due to bacterial invasion the passive form of hyperemia is to be used, while for the non-bacterial conditions the active variety is applicable."

The beginner should always bear in mind the possible danger of manipulating the blood stream, and at first limit his endeavors to early acute and subacute inflammations, especially those that ordinarily give a good prognosis. Furuncles, carbuncles, paronychias, felons, mastitis, lymphadenitis, etc., are all disorders in which suction can be employed with great benefit. Diffuse inflammatory infiltrations, unaccompanied by softening, and especially when the streptococcus is believed to be the causative organism, are not suitable for the treatment. If these are accompanied by fever and other evidence of constitutional disturbance, or if the process is rapidly spreading locally, passive hyperemia only does harm. In wide open accidental and operative wounds the method is of value. In general, it may be stated that disease of bone is very rebellious to the treatment, as it is, however, to any other method, because of the impossibility of producing any degree of œdema in the dense tissue.

*Tuberculous Arthritis.* In the treatment of this affection, as well as in all forms of surgical tuberculosis, passive hyperemia alone must be used and never hot air. The treatment aims slowly to produce a connective-tissue overgrowth, which replaces the tuberculous granulations; consequently the method requires much patience in its application, as frequently twelve or fourteen months are required to produce a cure. Some recent researches by Felegyhazi<sup>23</sup> show that in tuberculous sinuses examined microscopically the effect of passive hyperemia is to produce an increased formation of connective tissue. He believes that while phagocytosis is active in suppressing any mixed infection present, the result of the treatment depends upon the walling in of the tuberculous foci by the connective tissue. He also pertinently remarks that he is uncertain, until further experiments have been carried out, whether these submerged bacilli are eventually destroyed, or whether a trauma may set them free at a future date. The bandage is applied about the thigh or arm sufficiently tight to produce a bluish-red coloration, and, as a general rule, should remain in place for one hour twice daily. This may be decreased if found necessary or may be increased to two hours twice daily if better results are obtained by the longer application. Occasionally it may be found advisable to stop the hyperemia for a few days if the condition remains stationary. Great care should be taken of the part of the limb where the bandage is being applied, frequent changes of the point of application and gentle massage with oil being advisable. While complete immobilization is to be avoided, the patient should not subject the limb to any weight or strain, particularly in the early

stages. Cold abscesses frequently occur and must be opened as soon as detected, treated by the suction glasses in the manner described previously, and protected from contamination. As contra-indications, may be mentioned commencing amyloid disease, advanced phthisis, large abscesses filling the whole joint, faulty position of the joint with bony ankylosis, and "arthritis tuberculosa exsudativa" (hydrops). Several years ago Bier claimed 88 per cent. of cures in the hand and wrist, 72.7 per cent. in the elbow, 61.5 per cent in the foot and ankle, and 23 per cent. in the knee condition. The cold abscesses arising from Pott's disease of the vertebræ should not be subjected to suction unless it is absolutely necessary to open them, when the cups may be used to prevent mixed infection.

*Gonorrhæal Arthritis.* This disease is considered one of the most favorable for hyperemic treatment, not only because of the good result ultimately obtained, but also because of the early relief of the excruciating pain with which it is accompanied. It requires considerable judgment in interpreting whether good or harm is resulting and the method must be used with caution. The bandage should be applied twice in the twenty-four hours for ten or eleven hours each time, and during the pauses the œdema must be made to disappear by elevation and gentle massage, at which time the effect of treatment must be carefully scrutinized. Distention of the joint with pus or seropurulent fluid must be prevented by aspiration followed by irrigation with saline solution. Baetzner<sup>24</sup> reports 40 cases so treated in Bier's clinic, in which the duration of the condition was shortened, pain promptly relieved, early immobilization obtained, and ankylosis prevented in all the cases. Local treatment of the posterior urethra, prostate, etc., should, of course, be carried out at the same time.

Sufficient information is given in the preceding paragraphs to enable the practitioner to understand the principles and mode of application of this method of treatment. Especial emphasis must again be laid upon the dangers which may occur by its indiscriminate and unskillful use in acute infections, and, on the other hand, praise must be given in no stinted manner to the efforts of Bier to bring the method to the attention of the medical world. For sixteen years he has persistently advocated the use of hyperemia, both active and passive, and now, as the successor to von Bergmann at Berlin, he is in a position to command attention. In any inflammatory lesion where exudate, necrotic or plastic, is present, or whenever bacterial invasion of the tissues requires to be checked, the method is of more or less distinct value if it can be applied, but it must simply be regarded as an adjuvant to other older and well-known methods, and not as a panacea for all ills.

<sup>24</sup> Deut. Zeit. f. Chir., 1908, xciii, Heft. 1.

## THE DIAGNOSIS AND SURGICAL TREATMENT OF INGUINAL HERNIA.

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HAVING in a previous paper<sup>1</sup> discussed the etiology and pathology of inguinal hernia, we purpose now to discuss the diagnosis and surgical treatment, directing attention first to reducible and then to irreducible hernia.

**DIAGNOSIS.** A reducible hernia is either complete or incomplete. If it descends into the scrotum in the male, or the labium in the female, it is a complete hernia. If it remains in the inguinal canal, it is an incomplete hernia or bubonocoele.

There are a few things that may be confounded with an incomplete hernia. No doubt a retained testis and hydrocele of the cord are the two conditions most likely to give trouble. If the scrotum be examined carefully and it is ascertained that the two testes are where they should be, then, of course, an ectopic testis is eliminated. If, on the contrary, one is absent, the diagnosis is reasonably clear.

A hydrocele of the cord may easily be mistaken for a hernia, yet there are differential signs which should keep one from going astray. While both hydrocele of the cord and hernia give an impulse on coughing, there is a difference in the character of the impulse. In hernia the impact is caused by a more or less solid body coming in contact with the finger. It will vary somewhat according as the hernia is of the omentum or of the gut; but in either event, it will be different from the peculiar impulse given by a fluid, as in hydrocele of the cord. Then, again, hydrocele gives fluctuation, which is not the case with hernia. Moreover, the hydrocele is tense, pyriform in shape, and gives evidence of a tightly distended sac, which again is not the case with hernia. Furthermore, hydrocele of the cord is far more common on the right side than on the left. This is also somewhat true of hernia, but the disproportion is not so great as it is with hydrocele. Generally, in reducible bubonocoele the tumor disappears when the patient is in the recumbent position. Hydrocele of the cord usually does not.

In a complete reducible hernia there are several conditions that

may with difficulty be differentiated. Those most likely to give trouble are the congenital hydrocele, varicocele, and varix of the saphenous vein. Congenital hydrocele is undoubtedly more likely to cause difficulty in its differentiation than anything else. In both conditions the tumor reduces itself, or disappears, when the patient lies down; there is also an impulse on coughing in both, but the impulse is due to a more or less solid substance in hernia and to a fluid in hydrocele; there will be fluctuation in a hydrocele, but none in a hernia. The one crucial test, and by it one can always differentiate between the two, is that while both tumors disappear when the patient is in the recumbent position, if the finger be placed over the inguinal ring and the patient instructed to stand up, the hernia does not descend, but the hydrocele speedily reappears, because the fluid gets past the finger, whereas the more solid contents of the hernia do not.

Varicocele may easily be confounded with hernia. The last two cases of varicocele operated upon by one of us were diagnosed as herniæ by competent physicians. Hernia is very often, indeed in the majority of cases, on the right side; varicocele is nearly always a left-sided affection. Moreover, varicocele is an affection of adolescence, being very common between the fifteenth and twenty-fifth years. Hernia, on the contrary, is common in very young children and in old age. Still, however, there will be many herniæ encountered in young men, in whom varicocele is frequent. Both disappear when the patient is recumbent; both tumors give a distinct impulse on coughing, but the impulse is different. A more or less solid substance causes the impact against the finger in hernia, whereas varicocele is recognized by the soft purring made by the blood which is forced through the vessels against the finger. Then again, the descent of a hernia can be prevented when the patient is erect by pressing the finger over the internal ring and making pressure. The return of the varicocele, however, cannot thus be prevented.

A varix of the saphenous vein might, but should not be, mistaken for an inguinal hernia, though it is very often mistaken for a femoral hernia. The same rule applies to making the patient lie down, placing the finger over the internal ring, and asking the patient to stand erect. The hernia does not descend, whereas the varix speedily reforms. Again, varix of the saphenous vein nearly always is accompanied by varicosity of other veins lower down in the leg. Hence, if one only examines carefully, there should be no trouble in differentiating between either a femoral or inguinal hernia and a varix of the saphenous vein.

As difficult as it may be to recognize reducible hernia, incomplete or complete, it is far more difficult at times to differentiate between irreducible hernia and other conditions which oftentimes simulate it. The condition which is more likely to confound one than any-

thing else is hydrocele. A large number of cases of hydrocele are treated for hernia, and vice versa, and although it does not make so much difference if one treats a hydrocele for a hernia, it makes every difference if one undertakes to do for a hernia what is often done for a hydrocele. Therefore, we must be able to differentiate between these two conditions.

The swelling in a hernia begins above, in the inguinal canal, and descends into the scrotum. The swelling in a hydrocele begins below, in the tunica vaginalis, and extends upward. The testis in a complete hernia is forced to the bottom of the scrotum. In hydrocele it is situated posteriorly and at the junction of the lower and middle thirds of the scrotum. A hernia gives a distinct impulse on coughing; a hydrocele gives no impulse. A hernia is opaque to light; a hydrocele is more or less translucent, though in a hydrocele with a thick sac there may be little or no translucency. A hernia gives no fluctuation; a hydrocele does give fluctuation. The tumor in a hernia descends well into the scrotum and hangs down straight between the legs. A hydrocele is pyriform in shape and stands out more or less from the body.

Another condition, one that we should place next to hydrocele, which may give trouble, is orchitis, either acute, subacute, or chronic. The exquisite tenderness and other local evidences of inflammation, the general fever, and particularly the history of the case—that is, that it follows either trauma or infectious disease—ought to keep one from making an error in differentiating between hernia and orchitis. In the subacute or chronic varieties, however, there will be no redness of the skin and other evidences of local inflammation, and no accompanying systemic fever; hence the difficulty is greater. But the history of the case, there having been certain predisposing causes, such as gonorrhœa, tuberculosis, or syphilis, will largely prevent a mistake in diagnosis. Moreover, the testis, when enlarged, nearly always gives pain, oftentimes a peculiar nausea and faintness which follows handling the organ, and that in itself is most suggestive. Then, there is no impulse on coughing in an enlarged testis; there is always an impulse in hernia.

Another condition which might be mistaken for hernia is hematocele, or blood in the scrotum. It is not an easy mistake to make, and we believe that the books exaggerate the liability to err in this case. The history of a hematocele shows that it is nearly always sudden, and is caused by a blow, a kick, or trauma of some kind. Therefore, the tumor rapidly forms, and in addition there will very generally be an amount of discoloration of the part, which will at once enable one to recognize that there is blood beneath the skin.

In an irreducible hernia there will be either omentum, intestine, or both, retained in the sac, and, moreover, the contents will be prevented from returning to the abdomen even when the patient lies down, though an attempt is made to effect reduction by taxis.

Adenitis may also be easily confounded with irreducible hernia. The acute variety will, as a rule, give little trouble, because the exquisite tenderness of the inflamed lymphatic glands, the accompanying redness and signs of inflammation, the systemic fever, and above all, the history of the case showing that there has been acute infectious disease, point clearly to the nature of the affection. In the more subacute condition, though, particularly in tuberculosis, when there are one or more glands fused together, one might easily make a mistake. The history of the case; the fact that one can, as a rule, satisfy one's self that the enlarged glands are *near*, but not right *at* the external ring, and that the little finger can be insinuated into the inguinal canal, showing that it is empty in adenitis, whereas it will be occupied by the sac in a hernia, should prevent any mistake. It must be remembered that the neck of the sac in hernia must be internal to the spine of the pubis, whereas in adenitis the enlarged glands will nearly always be to the outside of the external ring.

Another condition that possibly will not be thought of is lipoma, or fatty tumor. The dough-like, inelastic lipoma at times may very closely simulate an irreducible omental hernia, for in such a hernia we have the same kind of tissue to deal with, to wit, fat. The lipoma, however, is more movable and situated in all probability more or less remotely from the inguinal canal. Its very location should enable one to recognize that it is a lipoma and not a hernia. Then, again, lipomas in this location are extremely rare; herniæ, very common.

Another condition that should always be thought of is cold abscess. Cold abscesses point very frequently at the inner aspect of the thigh. They are more likely to be confounded with a femoral than an inguinal hernia, because they usually point below Poupart's ligament; but they may point above Poupart's ligament, and then one may confound them with an irreducible inguinal hernia. What is the difference between them? In the first place the impulse on coughing, while marked in both, is different in a way. The hernia gives an impulse due to a more or less solid body. In abscess there is fluid, so that fluctuation may be elicited, whereas in hernia it cannot be obtained.

But there is a better way to differentiate between them. With the patient in the recumbent position, make very deep pressure with one hand over the lower part of the abdomen and with the other hand palpate the swelling. If it is an abscess, the fluid will disappear. It does not disappear into the abdominal cavity, however, but passes backward and upward behind the peritoneum; and then, as the swelling below is manipulated with one hand, and that in the loin with the other, a decided sense of fluctuation is obtained, which at once indicates that the two communicate.

There is also another way: examine carefully, and it will nearly

always be found that a cold abscess is accompanied by disease of the bones, showing itself either as spinal curvature or disease of the ilium. In other words, a cold abscess means accompanying disease of the bone somewhere; and if it is looked for, it will be found.

As difficult as it may be to differentiate between the foregoing conditions, there may be greater difficulty in differentiating between an irreducible inguinal hernia and an irreducible femoral hernia. In a stout, fleshy woman the diagnosis is especially difficult to make. There are two or three ways by which the two conditions can be differentiated. In an inguinal hernia the tumor appears above Poupart's ligament, because it must come out at the external abdominal ring. In femoral hernia it appears below Poupart's ligament, emerging at the saphenous opening. But while that is true, the hernia in the femoral variety is prevented from descending by the fascia lata. Therefore, it rolls up in the direction of least resistance, and soon gets above Poupart's ligament. Even so, one can tell the difference if one is careful. Place a finger on the spine of the pubis, which is external to the ring. In an inguinal hernia the neck of the sac must be, and can only be, internal to the finger. In femoral hernia the neck of the sac is well external to the finger, and at times may even be pulled out almost as far as the spine of the ilium. A third test is made by examining the inguinal canal with the finger, which is inserted into it through the external ring. In femoral hernia the canal will be found to contain only its normal contents, either the spermatic cord in the male, or the round ligament in the female. In an inguinal hernia, however, the inguinal canal is occupied by the sac and hernial contents.

Having thus gone over the most important diagnostic considerations, we will now discuss the several varieties of hernia which may be confounded one with another.

By an obstructed hernia is meant one in which the function of the gut is interfered with—and in a vast majority of instances it is the large gut which is affected—the intestine being distended with more or less hardened feces. What will be the symptoms of obstructed hernia? All the signs and symptoms of irreducible hernia in the first place, and in addition thereto, certain signs more or less characteristic of obstruction. Thus, nausea will nearly always be present and frequently there will also be vomiting, which, however, is easily controlled by withholding food. In other words, the patient empties the contents of the stomach, so that if food is withheld, vomiting ceases. There is more or less pain in an obstructed hernia. The pain, however, is never severe, but it is a more or less general, vague, indefinable sense of discomfort.

There is an impulse on coughing in an obstructed hernia, yet it is different from the impulse of irreducible hernia. It is slight, may be found only at the neck, and in trying to elicit this sign one should delicately grasp the neck of the hernia and ask the patient

to cough, when an impulse will be felt. Sometimes this is the only possible way that one can differentiate between an obstructed and a strangulated hernia.

There will be constipation in an obstructed hernia, but the constipation is relative, not absolute. The lower bowel may act more or less spontaneously, but it never empties itself, only allowing a certain portion of its contents to pass. There will always be passage of gas, however, and if a clear history of this can be elicited, we have another valuable sign which tells plainly enough that the condition is obstruction and not strangulation—if we except the extremely rare variety, Richter's hernia.

Now as regards inflamed hernia. A patient has an irreducible hernia; he receives a blow, a kick, or he falls, for instance, astride the rung of a ladder—in other words, sustains trauma. There will be certain signs in an inflamed hernia that one would not expect in either irreducible or obstructed hernia. Manifestly, the pain will be greater, and it will be local. It will not be that vague, ill-defined, general pain, characteristic of obstruction; but it will be largely confined to the inflamed sac and its contents. The hernia will also be, perhaps, exquisitely tender to the touch, and if the temperature be taken, it will be found that the patient has fever, not marked, but an elevation of a degree or a degree and a half. There will also be an impulse on coughing, and other symptoms that will be practically the same as in obstructed hernia.

How are we to recognize strangulated hernia? Of all herniæ, this is the most important to appreciate and treat promptly. An obstructed hernia may cure itself, an inflamed hernia may likewise do so, but a strangulated hernia practically never does so, and death results without surgical intervention. How can it be diagnosticated? In the first place, an obstructed hernia borders closely on strangulation. Hence it is not surprising that an obstructed hernia of today may become a strangulated hernia tomorrow. In other words, obstruction merges into strangulation, because the hardened feces accumulate in the distended gut and not only interfere with the function thereof, but, if it be very much distended with hardened feces, its circulation at the neck may be interfered with by pressure, and when both function and circulation are interfered with strangulation ensues.

As soon as strangulation takes place there will be, as a rule, rather pronounced shock. We say "as a rule" advisedly, for the reason that we do not believe it is always well marked. We are satisfied that the text-books nearly all overemphasize the degree of shock present in strangulated hernia. Certainly in a large percentage of the cases seen by one of us there was no shock at all. Shock may possibly pass away before the physician, especially the surgeon, is called in. We doubt not if one could see a strangulated hernia early, as soon as it begins, that there would practically



always be more or less evidence of shock. It is easy to understand why that is so. Shock manifests itself by a subnormal temperature, weakened pulse, cold, clammy skin, pale countenance, and pinched features. Almost at once the patient begins to vomit—and here the character of the vomiting is very different from that which occurs in obstructed hernia. It is projectile, continues in spite of everything that is done, the patient first vomiting the contents of the stomach, later on bile, and later still the contents of the intestines.

There will be a peculiar pain about a strangulated hernia. It is uncertain and variable, at times so great as to be accompanied by marked shock, at other times scarcely present at all. It may be steady or intermittent, but usually is intermittent and colicky in character.

**TREATMENT.** We will consider, first, the treatment of the complications of hernia. The first is irreducibility. We may say in general, that all irreducible herniæ demand a radical-cure operation, unless there are distinct contra-indications to any operative procedure. If the patient be very old and the hernia very large (more frequently the case in umbilical rather than inguinal hernia), an operation may be exceedingly dangerous. Then, again, if the patient has disease of the kidneys, or other organic disease, it is better not to operate, but to be content with supporting the hernia by means of a bag, a hinged-cup truss, or other suitable appliance. But without such complications an irreducible hernia invariably calls for an operation, because of the fact that it may in time become inflamed, obstructed, or strangulated.

It should be remembered that such herniæ are necessarily exposed to all forms of traumatism and that a fall or blow may cause either rupture of the gut, inflammation, or strangulation. We have known rupture of an irreducible hernia to occur as the result of the kick of a horse, and we have not infrequently seen inflammation excited by various kinds of trauma, particularly by ill-fitting and injudiciously worn trusses. So, while one may hesitate to perform a radical cure operation for a reducible hernia, and rightly so, there is practically no choice in the irreducible variety. The patient's safety will be best subserved by an operation in which there is practically no danger. Moreover, his comfort will be enormously enhanced thereby; hence it is vastly more important to operate upon irreducible than upon reducible herniæ.

The next complication is obstruction, or so called incarceration. How is it to be treated? In the first place, it should be remembered that obstruction is nearly always preceded for a greater or less time by irreducibility. The hernia is first irreducible, subsequently becoming also *obstructed*. Therefore, in its treatment one should have in mind relief to the obstruction, and not overcoming irreducibility, because that is practically impossible. This is not to be done by purgatives, as might be supposed, but by high enemas

of warm olive oil, so that the feces may be softened, and in this way the obstruction overcome, it being due, as a rule, to hardened feces in the sigmoid or some other portion of the large gut. It is only after the large intestines have been moved well by enemas that purgatives are to be considered at all. Even then a non-irritating purgative such as castor oil is indicated. A restricted diet, consisting of food with little residue, is of the utmost importance if food is to be given at all.

Inflamed hernia is to be treated by absolute rest in bed and by local applications, either hot or cold. With the average adult who is more or less vigorous cold is preferable to heat. An ice bag over the hernia gives great comfort and lessens the inflammation. In old people, however, cold applications are of questionable utility. The vitality of such patients is below par, and the prolonged or injudicious use of cold applications may easily cause gangrene in patients of advanced age. Therefore, when in doubt as to whether cold or hot applications should be used, one had better decide in favor of the latter. They should be changed frequently, every five minutes, so as to get the best possible results. In addition to local applications, enemas may be employed, as in obstructed hernia. One may be driven to give what one would hardly think of giving in an obstructed hernia, that is, a small amount of opium to relieve pain.

If inflammation passes on to strangulation, or if there is doubt as to whether or not strangulation has occurred, the safety of the patient will be best subserved by making an incision, establishing drainage, and inspecting carefully the condition of the gut.

We will finally consider the most important of all accidents associated with hernia—strangulation. There are two ways of treating strangulated hernia. One is by manipulation, or taxis, as it is called; the second is by herniotomy, or cutting the constriction and relieving the imprisoned gut. The usual method is to employ taxis in practically all strangulated herniæ before resorting to herniotomy. Formerly, this practice was well nigh universal; in pre-antiseptic days it was used far more extensively than it is at the present time, because of the mortality following herniotomy. There is, however, a growing tendency with many surgeons to esteem lightly the value of taxis; moreover, its dangers are manifest, and if employed, it should only be to a very limited extent. In certain cases taxis should not be employed at all; thus, if the hernia was previously irreducible, it is manifestly absurd to use taxis, for if irreducible before it became strangulated, it would be impossible to reduce it with strangulation superadded.

Then, again, if the hernia has been strangulated for some hours, particularly if it be a small, tense hernia, the danger of attempting to reduce it by taxis is very great indeed, since taxis, however delicately made and however skilled the surgeon employing it,

may cause the gut, already softened by inflammation and distended by feces and gas within, to rupture; this accident would almost certainly be lethal. If the hernia has been strangulated for some hours, taxis would be not only futile, but positively dangerous. This is true of all herniæ, but it is especially true of a small, tense, femoral hernia.

How often does taxis succeed in reducing a strangulated hernia? In thirty years' experience one of us has reduced but one undoubtedly strangulated hernia by taxis. Many others which were thought by those in attendance to be strangulated, but which in reality were not, have been reduced. The idea that one gets from reading text-books as to the value of taxis is absolutely wrong, and in the judgment of modern surgeons it is to be employed with the utmost caution, if at all, and only in well-selected cases.

There are certain accidents that may follow taxis. In the first place a loop of intestine which is nipped tightly at the neck and distended with gas may very easily rupture, just as a tightly distended rubber bag may burst when incautiously pressed upon. Second, reduction *en masse* may follow. By this is meant that an injudicious attempt at reduction has resulted in both sac and contents being pushed back into the abdominal cavity, but that the constriction which is causing the strangulation is unrelieved. In other words, although the tumor disappears into the abdomen, the symptoms of strangulation continue, and it is evident that the constriction was within the sac, and consequently has not been relieved. In such circumstances the patient dies unless abdominal section is performed. Third, the gut may be so injured, although not ruptured, at the time it goes back into the abdominal cavity, that as a result of such bruising and the inflammation which follows, there is subsequently a perforation of the gut, which necessarily means a fatal peritonitis. One of us has personal knowledge of a case in which spontaneous rupture of the intestine occurred a week after reduction by taxis. This was demonstrated at autopsy.

Taxis should never be employed until the consent of the patient for a herniotomy has been obtained, in the event of it proving fruitless. The relaxation following an anesthetic is necessary for a successful attempt at taxis. Should such an attempt prove unsuccessful, as it generally will, it is manifestly unwise to allow the patient to come from under the anesthetic before resorting to herniotomy. Taxis, if employed at all, should not be continued more than five minutes. If successful, and the hernia is an enterocele, it disappears into the abdomen with an audible gurgling sound, indicating reduction. If an epiplocele, there is no noise, but a gradual disappearance of the swelling.

The best way to employ taxis is gently to grasp the neck of the sac between the thumb and index finger of the *left* hand, and then, with the thumb, index, and middle fingers of the *right* hand, the

fundus or expanded portion of the swelling is gently manipulated. At first it is pulled upon for the purpose of disengaging the neck. Afterward it is carefully compressed so as to displace feces and gas, thereby reducing the volume of the hernia, so that the imprisoned gut and omentum may escape.

**HERNIOTOMY.** By herniotomy, or, as it is sometimes called, kelotomy, is understood cutting the constriction and replacing the damaged gut or omentum, if they are in proper condition, into the abdominal cavity.

There is little danger in the procedure, scarcely more than in a simple radical-cure operation; but the condition of the patient and hernial contents is very different, and this explains the mortality. If the operation is delayed, as is so often the case, owing first to a belated diagnosis, and second, to procrastination on the part of the physician, the mortality is necessarily great. If performed after twelve hours, such damage to the intestine will have ensued that the mortality is not less than 25 per cent. If done after twenty-four hours, the mortality is 50 per cent. Therefore, the one thing to have in mind is to operate as soon as possible after the diagnosis is made. If a case is seen during the day, the sun should never be allowed to set before the operation is done. If seen at night, even though it be in the "wee sma' hours of morn," the sun should never be allowed to rise before relief is given.

*Technique.* The incision should be made above and parallel with Poupart's ligament—in other words, over the *neck*, where the strangulation in all probability exists, and not low down in the scrotum. In the first place, one can get at and relieve the constriction better; in the second place, the field of operation is a more aseptic one.

Cut carefully down until the sac is reached, it being recognized without difficulty by its lustre and the arborescent arrangement of its bloodvessels. It should not be difficult to differentiate between the thin sac above and the intestine beneath, as the latter is thick, softer, darker in color, velvety to the touch, and wanting in the larger bloodvessels found in the sac. If in doubt, delicate palpation will usually elicit fluctuation beneath the sac, due to fluid almost invariably present. In certain cases of doubt, a hypodermic needle may be used most judiciously, being introduced in a slanting direction, so as to avoid probable injury to the gut beneath.

The sac having been identified, it is to be freely laid open to the extent of the superficial wound. Fluid at times escapes, and its color, odor, and general appearance indicate fairly well the condition of the imprisoned bowel. If clear and free from odor, the probability is that little damage has resulted. If the strangulation has lasted several hours and the constriction is tight, the fluid may be more or less brownish, or dark colored, and contain flakes of lymph. Even so, the chances are still favorable. If, however,

the fluid be very thick, dark and ill-smelling, it is suggestive at least of impending, if not actual, gangrene.

The next step is cutting the constriction. In inguinal and umbilical hernia this can be done in two ways: (1) From without inward; (2) from within outward. Although the latter method has been, and still is, very generally practised, it is less safe for several reasons than cutting from without inward. The latter has the advantage of being done deliberately under the eye. Therefore, damage to the gut is unlikely. If the constriction is cut from below upward, the distended and inflamed bowel may be easily punctured by either the grooved director or knife as they are introduced beneath the constriction. We consider this an important step in the operation of kelotomy and insist that the constriction both in inguinal and umbilical hernia should always be cut from without inward, for not only is the bowel less endangered thereby, but there is considerably less risk from hemorrhage. One is open, the other subcutaneous surgery. Unfortunately, the old method of cutting from within outward must, for anatomical reasons, necessarily obtain in femoral hernia.

The only vessels endangered in strangulated inguinal hernia are the deep epigastric artery and vein. These will be avoided by cutting the constriction in a direction parallel to the vessels, that is to say, directly upward. True it is that one could safely cut externally in indirect hernia, internally in direct hernia, but as it is simply impossible to say definitely in every case that the hernia is either the one or the other, the constriction should be cut in a direction equally safe for both.

Where will the constriction usually be found? It is most frequently at the external ring. We desire to emphasize this fact, as many of the older writers insisted too much upon the probability of the strangulation being at the internal ring.

The constriction having been relieved, the appearance of the strangulated loop of intestine at once improves both in color and temperature. In truth, a deep mahogany or rose color may quickly pass away as soon as arterial blood is allowed to enter and, *pari passu*, the venous blood to escape. With a change in appearance will be a return to the normal temperature. Before relief of the strangulation, the gut is cold and clammy. If both color and temperature quickly improve, there is little risk in returning the extruded bowel to the abdominal cavity. Per contra, if after waiting ten minutes or longer, the bowel, though improving somewhat, still remains discolored, dull, lustreless, and its temperature sub-normal, there is at least a question as to its viability; therefore, if it is to be returned to the abdominal cavity, it should be anchored at the internal ring by placing a catgut suture through its mesentery, so that in case of subsequent perforation it may break *externally*, and not into the abdominal cavity. A better plan, in our judgment,

is to leave the herniated bowel outside of the cavity and to apply hot salt solution frequently for twenty-four hours. This not only favors its vitality, but certainly lessens the danger of general peritonitis.

If, after waiting a reasonable length of time, there is no apparent improvement in the bowel; in other words, if gangrene has already occurred, or the bowel is in such a softened seminecrotic state as to make one certain that it would be dangerous to return it to the abdominal cavity, two courses are open to the surgeon: (1) Resection of the gangrenous portion, followed by end to end anastomosis, or closure of the proximal and distal ends with lateral anastomosis; (2) establishment of an artificial anus.

Resection is ideal, more in consonance with surgical principles, and if the condition of the patient is good, the operator of more than average skill, and he has competent assistants, it should be first considered.

If, as is frequently the case, the patient is much reduced on account of prolonged vomiting, shock, and absorption of ptomaines, so formidable a procedure as resection of the intestine and restoration of the continuity of the alimentary tract may be out of the question. In such circumstances, the safety of the patient will probably be best subserved by making an artificial anus temporarily, hoping to close it later on. There are two ways of doing this. First, cut the constriction, pull down the intestine, excise the gangrenous portion, and suture both the proximal and distal ends to the skin. Another plan is to incise the intestine so as to let the gas and feces escape *without* cutting the constricting band. In this way, soiling of the peritoneal cavity is prevented, as gas and feces readily escape externally.

Very recently, one of us did this with success in a feeble old lady nearly eighty-seven years of age, who for years had suffered from a large irreducible epiplocele. Strangulation eventuated, being superinduced by the descent and nipping of a portion of the ilium; it having lasted from Tuesday morning until Friday at 3 A.M., the time of our visit and operation, gangrene of course, was to be expected. Both omentum and bowel were gangrenous. The former was resected, a piece larger than a fist being removed. The condition and extreme age of the patient not warranting resection and reestablishment of the continuity of the intestinal tract, an artificial anus was established by incising the gut and making free drainage. To protect the cavity against infection *the constriction was not cut*. All symptoms of strangulation were at once relieved, there being no further vomiting or pain.

Inasmuch as it is impossible to say whether or not the gangrene has extended beyond its apparent limits and *above* the constriction, this is necessarily surgery in the dark and, as a rule, not to be recommended.

There are many reasons why an artificial anus should not be established, except it be as a *dernier ressort*. In the first place, the thought of it is always one of repugnance to both patient and friends. Next, it presupposes the danger, discomfort, and loss of time incident to a second operation. Furthermore, if the herniated bowel be the jejunum or upper ileum—not infrequently the case—the patient must rapidly fail from malnutrition. We now appreciate the important role the upper intestine plays in digestion and that the stomach largely receives and prepares food for assimilation in the intestines below.

In spite, however, of the natural and surgical reasons for not making an artificial anus, the condition of the patient, his environment, and the want of the best surgical assistants may make it necessary. What is best for one case is certainly worse for another. Good surgical judgment must be shown, and nowhere in surgery does the personal equation count for so much.

Assuming a favorable case, one in which the bowel regains its normal condition after the constriction is relieved, herniotomy should always, when practicable, be supplemented by a radical cure. It is only a question of ten minutes longer under the anesthetic, and it eliminates all further dangers from the hernia. It should be carried out according to one of the approved methods, Bassini's being preferred.

The after-treatment of patients who have had strangulation is of the greatest importance. Vomiting has been so persistent that the thirst of such patients is well-nigh unquenchable. Therefore, water should be given in moderation as soon as the patient comes out of the anesthetic. Before he has done so, continuous enteroclysis should be begun. Not only is thirst relieved in this way, but the kidneys and skin are made more active, thereby eliminating poisonous products which have been absorbed. A little highly concentrated broth, albumin water, or milk may be given by the stomach as soon as they are likely to be retained.

The bowels should be allowed to act spontaneously, which they will usually do within twenty-four hours. Should such be not the case, an enema may be given. Purgatives by the mouth are dangerous, and should not be given, lest by their drastic action they cause damage to, or even perforation of, the bowel.

In the somewhat rare form of Richter's hernia, we think, on the whole, that an artificial anus would generally be indicated, for the symptoms of strangulation are not so severe, and, therefore, such cases will have lasted several days in all probability before they come to operation. Hence they will not be in a condition for resection with a restoration of the continuity of the alimentary canal, and an artificial anus is both easily and quickly established. It is, moreover, likely to be followed by spontaneous closure unless the knuckle of gangrenous intestine is large.

Having considered the treatment of irreducible, obstructed, inflamed, and strangulated herniæ, we will now state frankly our views concerning the treatment of the most common variety—reducible hernia.

The treatment is either mechanical or operative. While not denying the advantages and indications for mechanical, or truss, treatment, in well-selected cases, we wish to state most positively our belief that it is the treatment for the *exceptional*, not the average case. In other words, it is our opinion that mechanical treatment should only be used when there is some good contra-indication to operation. We say this for two reasons: (1) On account of the uncertainty and the potential dangers of truss treatment; (2) because the operative treatment is practically free from danger and almost invariably successful. We believe that during the last decade there has been a very decided change in professional sentiment concerning the value of mechanical treatment, and that trusses are being used very much less frequently than during the time when the radical cure operation was less satisfactory than it is at present.

Young infants, and very old people, especially those with bronchitis, arteriosclerosis, disease of the kidney, diabetes, etc., should usually be treated by mechanical rather than operative means. All others should, as a rule, be promptly submitted to operation. It seems utterly incongruous at the present time to advise a young adult, a middle aged man or woman, or even one in the youth of old age, to wear a truss rather than to submit to an operation having a mortality so small as to be negligible, and results almost invariably satisfactory.

Even those who fear a general anesthetic can be operated upon, cocaine or other local anesthetic being used.

Our operations in young children have been uniformly successful, and we do not hesitate to advise a radical cure after two years of age, and oftentimes, and for good reasons, sooner. Few mothers have the time, the intelligence, and the patience to get the best results from mechanical treatment. If such treatment is to be carried out imperfectly, it is worse than none at all. We have not found any more difficulty in securing primary union after operations in childhood than we have in adult life.

Believing, therefore, that too much attention is still given mechanical treatment, we shall say nothing concerning the different varieties of trusses, their applications, etc.

OPERATIVE TREATMENT. Interesting as it would be to begin with the first operation for the radical cure of hernia, following it by all of the various steps and advances which have been made in the evolution of the perfected operation of today, we hardly think it would subserve any useful purpose at this time. Many errors were made by those introducing new methods, largely on account of faulty anatomical conclusions. While not inclined to discredit



the efforts of earlier workers in this line, it must in all candor be said that no great advance was made until the introduction of the operation of Bassini in 1889.

The principal features of this method contemplate separation of the cord in the male, the round ligament in the female, from the sac; high ligation of the sac; removal of the sac; suture of the conjoined tendon or internal oblique and transversalis muscles above to the deep shelving of Poupart's ligament below, by which a new floor is made for the canal; transplantation of the cord, and suture of the external oblique muscle *over* the transplanted cord.

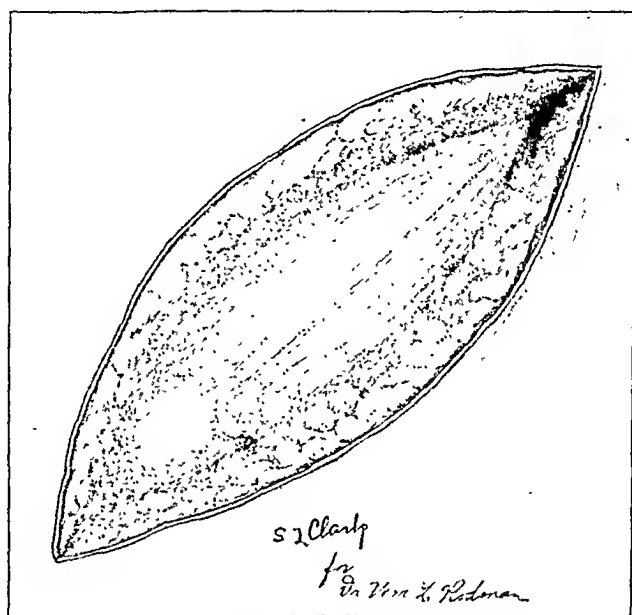


FIG. 1.—Showing the hernia presenting at the external abdominal ring after the skin and fascia have been divided and the aponeurosis of the external oblique muscle exposed. (Drawing made from sketches taken at Dr. Rodman's clinic, Medico-Chirurgical Hospital.)

In short, the inguinal canal is reconstructed (Figs. 1, 2, 3, 4, and 5.) Some of the above steps had been adopted by various operators, but with indifferent success. All, or nearly all, of them are essential.

There are some excellent surgeons who still retain the sac, but nearly all who do have a different method of disposing of it. It seems to us that it should always be removed, and that its retention, whatever may be done with it, constitutes a distinct menace.

The principles which Bassini advocated and caused to be accepted throughout the civilized world had been, it is true, followed and advocated in the main by Marcy, and perhaps others. While the very best results have been and are being obtained by Bassini's operation, there is undeniably a growing tendency among many operators not to transplant the cord in every case (Fig. 6).

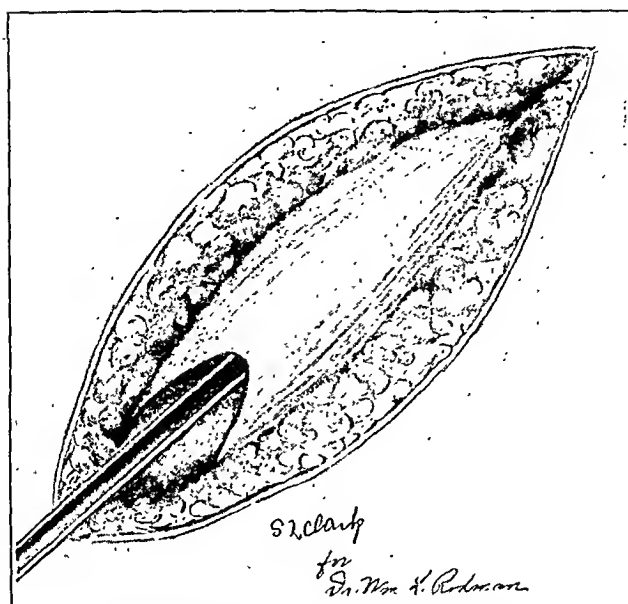


FIG. 2.—The inguinal canal is about to be opened by an incision made in the groove of a director which has been passed through the external abdominal ring. The structure to be divided is the aponeurosis of the external oblique muscle. (Drawing made from a sketch taken at Dr. Rodman's clinic, Medico-Chirurgical Hospital.)

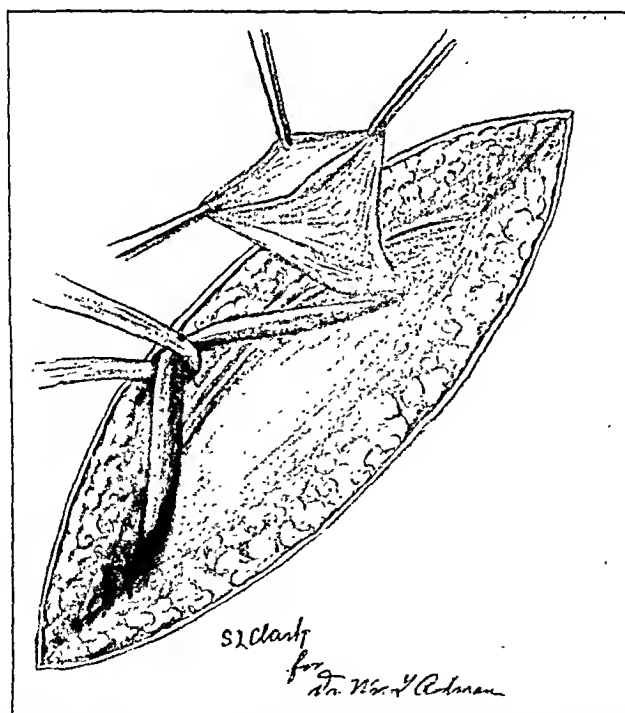


FIG. 3.—The sac of the hernia has been opened, the contents reduced, and the sac separated from the spermatic cord. (Drawing made from sketches taken at Dr. Rodman's clinic, Medico-Chirurgical Hospital.)

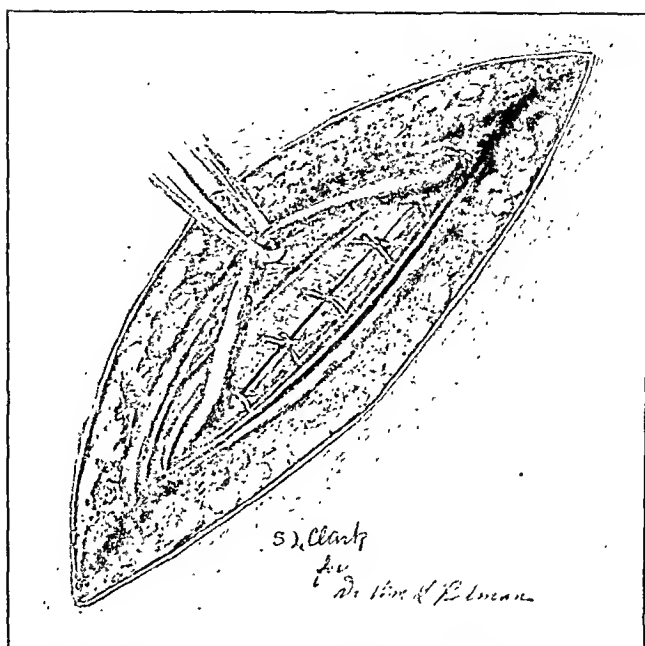


FIG. 4.—Showing Bassini's method of radical cure. The lower margin of the internal oblique muscle, together with some of the transversalis, has been sutured to the shelving margin of Poupart's ligament. The spermatic cord will be placed upon the new floor thus formed. (Drawing made from sketches taken at Dr. Rodman's clinic, Medico-Chirurgical Hospital.)

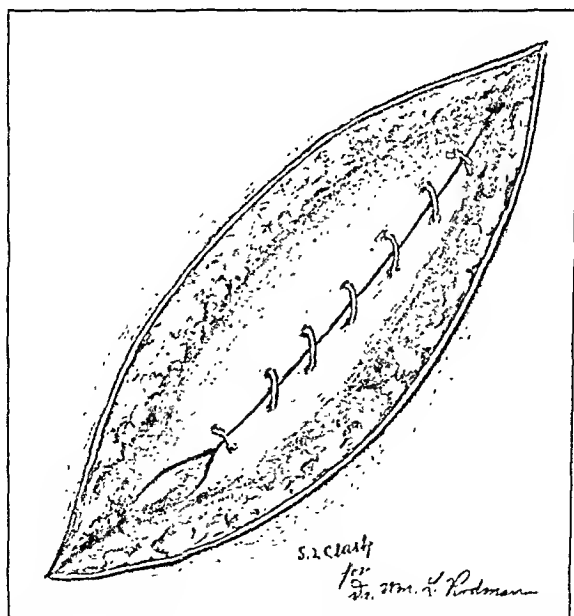


FIG. 5.—Showing the aponeurosis of the external oblique muscle sutured over the spermatic cord. (Drawing made from a sketch taken at Dr. Rodman's clinic, Medico-Chirurgical Hospital.)

It is our belief that transplantation of the cord has been followed by such uniformly good results that it remains to be shown that it is *unnecessary*.

During the last five years we have in many instances omitted this step of the operation, and, so far as we know, without recurrence of a single hernia. At the same time, we have operated on a very much larger number of cases in which the cord *was* transplanted with the most gratifying results. Clearly, the cord should *not* be transplanted when the hernia is accompanied by a retained testis, inasmuch as the cord is already too short.

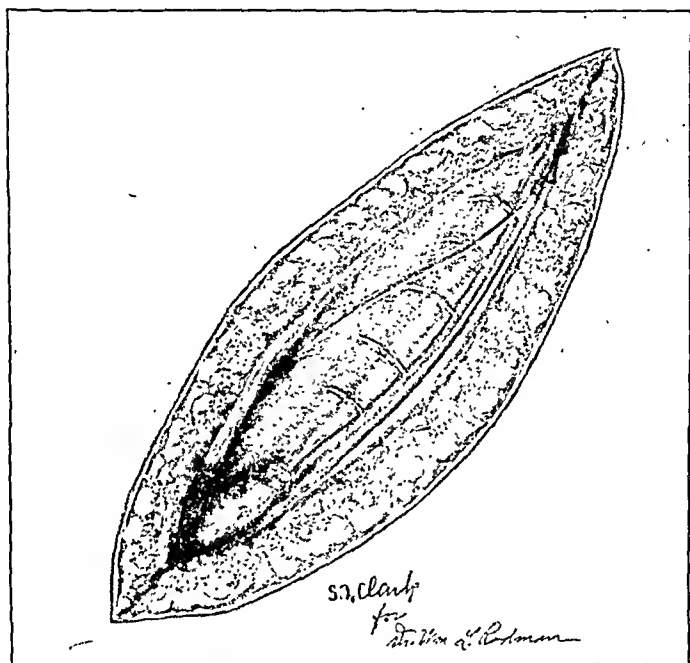


FIG. 6.—Showing the internal oblique and transversalis sutured to the shelving margin of Poupart's ligament without transplantation of the spermatic cord. (Drawing made from sketches taken at Dr. Rodman's clinic, Medico-Chirurgical Hospital.)

The frequent association of oblique inguinal hernia and retained testis is well known. Usually it is quite easy to bring down the testis (especially if the method of Bevan be employed), and to transplant it into the serotum. The former practice of sacrificing the organ is rarely justifiable now, as it is surprising how these very small, seemingly imperfect, testes develop and thrive when brought down into the serotum where they are relieved from pressure and constant irritation. We have operated on a number of these cases with the utmost satisfaction. The operation of Bevan is much the best.

Only a few weeks ago it was the privilege of one of us to re-examine a boy of seventeen years upon whom he had operated for retained testis eight years previously. At the present time the

transplanted organ is quite as large as its fellow. At the time of the operation, when he was nine years old, the testis was ill-developed and situated high up in the inguinal canal. In truth, it was so small and the cord so short, that the father of the boy, himself a physician, doubted the wisdom of the attempt to save the organ, and would have been better pleased had castration been performed. He continued to be pessimistic as to the outcome, and would so express himself at our meetings for several years subsequent to the operation. He now informs us that with the onset of puberty the testis began to enlarge, became firmer to the touch, and showed decided evidence of awakening. It is needless to say that he is delighted with the result.

One of us has had other cases quite as satisfactory since beginning to operate upon these patients more than twenty years ago. We think it necessary, and invariably do so, to follow such transplantation by a radical cure for hernia. The two conditions are frequently, if not usually, associated. Further, the patients in whom hernia has not developed are certainly more than ordinarily predisposed to it on account of the long dilatation of rings and canal by the misplaced testis.

It is our belief that too much has been written concerning the liability of retained testes to undergo sarcomatous change, and for this reason demanding castration. Twenty years ago one of us was of this opinion, having seen one such case, and being influenced by the literature of that day; hence he advised removal of one or two retained testes, believing that they were without function and a perpetual menace to life itself. We have advised and practised transplantation, however, in every case presenting itself during the past fifteen years.

More important than the question of transplantation of the cord are the ones of securing primary union and the use of absorbable sutures. In order to secure asepsis, we believe it almost indispensably necessary for operator and assistants to wear rubber gloves. Hemorrhage should be carefully arrested, lest a hematoma form and thus further the liability to infection.

If the veins of the cord are enlarged, we do not hesitate to resect them, and have done so in a fairly large number of cases. In a few instances a hydrocele has developed after this procedure, but we have never witnessed what others have seen, namely, atrophy of the testicle.

In addition to the principles embodied in the Bassini procedure, we employ in all direct, and in many indirect herniæ, transplantation of the anterior sheath of the rectus muscle, and believe it to be a most useful step (Fig. 7). Transplantation of the substance of the rectus muscle is not employed as a routine procedure. In operating upon a large congenital hernia in an adult whose inguinal canal was greatly widened, one of us recently turned

down a portion of the muscle, together with its anterior sheath, in the manner shown in Fig. 8, and then sutured the superficial

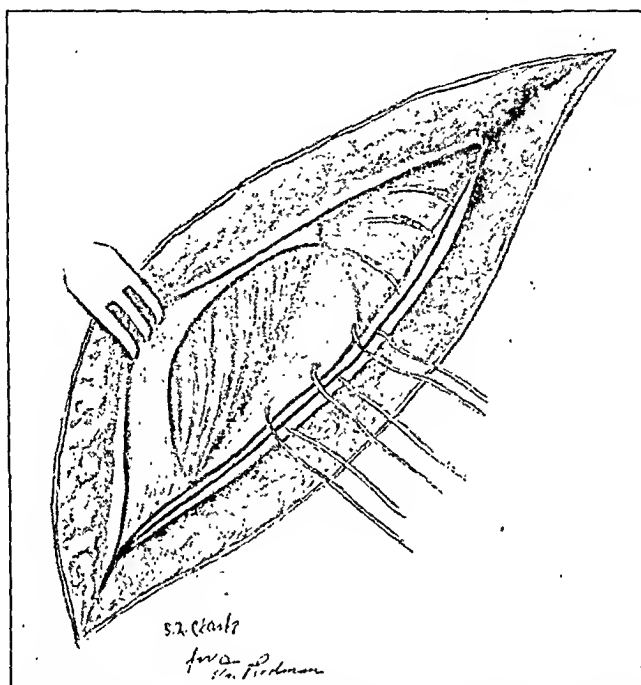


FIG. 7.—Transplantation of the sheath of the rectus muscle. (Drawing made from a sketch taken at Dr. Rodman's clinic, Medico-Chirurgical Hospital.)

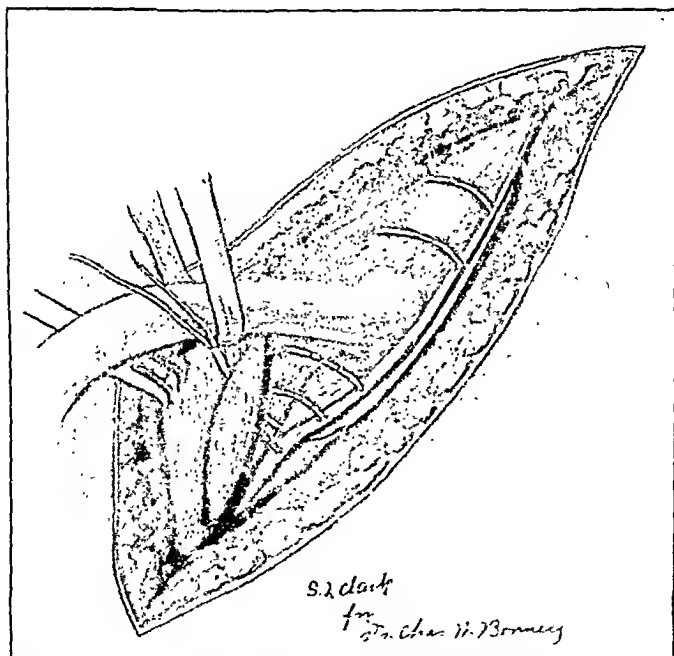


FIG. 8.—Showing a method of transplanting a portion of the rectus muscle as well as its sheath. (Drawing made from a sketch taken during an operation by Dr. Bonney.)

fascia to the cut margin of the rectus. It was hoped that this procedure would lend additional strength to the reconstructed canal even though the transplanted muscle atrophied.

In congenital hernia a tunica vaginalis testis may be formed in the manner shown in Fig. 9.

If the muscles are very much attenuated or stretched, overlapping, or the so-called imbrication in the manner indicated in Fig. 10, is practised. We believe this step one of the decided

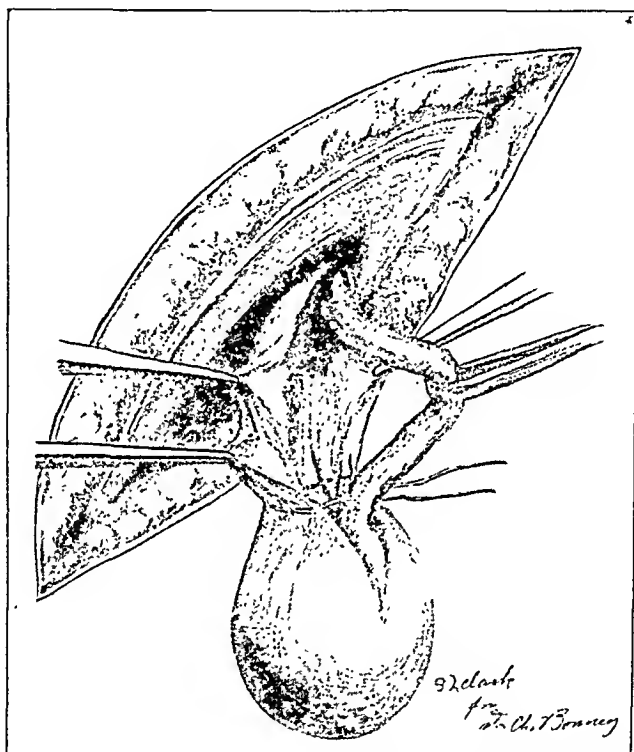


FIG. 9.—Showing a method of making a tunica vaginalis in cases of congenital scrotal hernie. (Drawing made from a sketch taken during an operation by Dr. Bonney.)

advances made in recent years. First introduced by Andrews, of Chicago, it has been variously modified by many operators.

We also preserve and make use of the cremaster muscle. In two direct and one indirect herniæ which recurred after the ordinary Bassini procedure, with transplantation of the cord, we re-operated successfully by transplantation of the sheath of the rectus. These and two others are the only five recurrences, so far as we know, in more than eight hundred operations for inguinal hernia. That other patients have suffered recurrences we do not doubt, but they have not reported themselves to us. We are reasonably sure, however, that no recurrence has taken place in any of our private

patients, all of whom have been followed and traced. No attempt has been made to follow up ward cases operated in the several hospitals with which we are connected.

There has been no mortality from the operation. One case was lost after an operation for a large umbilical hernia in a stout woman who weighed two hundred and fifty pounds. Death occurred at the end of three weeks when the patient was about ready to leave for her home. She died one morning about three o'clock after an illness of a few moments. Death was evidently due to embolism. Many such cases have been reported, as embolism seems to be somewhat more closely associated with hernia than would appear reasonable.

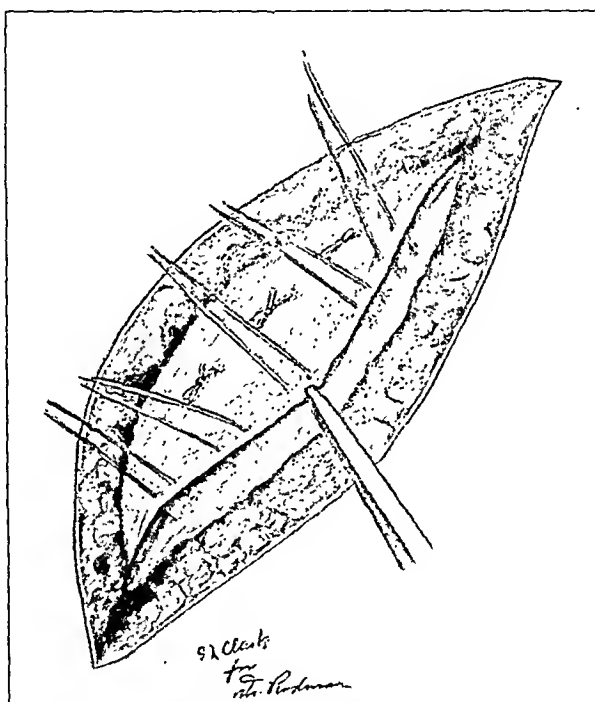


FIG. 10.—Showing overlapping of the aponeurosis of the external oblique muscle from above downward. The upper sutures are inserted from without inward. (Drawing made from sketches taken at Dr. Rodman's clinic, Medico-Chirurgical Hospital.)

Formerly, for instance, fifteen years ago, we believed it necessary to keep patients in bed four weeks, but an increasing confidence in the operation has caused us to shorten the interval until now we think a fortnight in bed long enough. We never advise that a truss or elastic belt be worn. We do, however, insist that a rather firm spica bandage, made of flannel, applied over a compress of gauze, be worn for several weeks after the patient gets out of bed. Such support not only secures the comfort of the patient, but we



believe is a safeguard against recurrence. Wound healing does not take place with the same rapidity and certainty in all cases. Therefore, it seems to us that this precaution should be taken.

**DOUBLE HERNIA.** Not infrequently patients present themselves with a hernia on both sides, and it becomes a question as to whether one or both sides shall be operated on. As the duration of the operation for radical cure does not, as a rule, consume more than ten or fifteen minutes, there is no reason why both sides should not be operated at the same time. It is our invariable custom to follow this plan, and in addition not infrequently perform an appendectomy, circumcision, or radical cure for varicocele, should such operation be necessary. Little is added to the danger of the operation either from the anesthetic or shock if the procedure is completed within an hour.

In cases in which a general anesthetic seemed contra-indicated, we have also operated with entire satisfaction under spinal anesthesia or cocaine used locally. We do not believe with some, however, that this operation should usually be done under local anesthesia, as the time is prolonged and the dangers of wound infection proportionately increased.

One of us has operated under spinal anesthesia in quite a number of cases with perfect satisfaction, and do not hesitate to make use of it when there are contra-indications to general anesthesia. There are times when we have found it very convenient to have the co-operation of the patient and to have him cough or strain at the desirable moment. For the same reason we often employ spinal analgesia in operations on the rectum, and find it most helpful. One of us has performed a radical cure for hernia and then sutured both external and internal sphincters of the rectum (which were cut by a farmer's falling astride a pitchfork) under one injection of stovaine. Notwithstanding the fact that more than an hour was necessary to do the hernia operation and then carefully to suture first the internal and then the external sphincters, the entire operation was painless. Had it not been for the coöperation of the patient, it would not have been possible to suture the internal sphincter muscle so well. Incontinence of feces, which was complete before operation, was entirely and at once relieved.

THE DIAGNOSIS OF CANCER OF THE INTESTINES.<sup>1</sup>

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IN considering the cause of any chronic digestive disorder, cancer can never be left entirely out of account. It is always a possibility in any patient over thirty years of age; always the most likely explanation in any patient over forty; and never can be eliminated from the calculation until after all the evidence has been obtained and carefully weighed. But cancer is not equally distributed throughout the digestive tract. In fact, it exhibits a decided partiality for some regions and a decided neglect for others, so that a knowledge of this peculiarity aids us if we can trace the origin of the symptoms to a certain organ or a certain region in the abdominal cavity. With stomach symptoms predominant, cancer is particularly to be borne in mind in any chronic case, for the great frequency of cancer of the stomach can never be forgotten. But with intestinal symptoms the striking ones, cancer is less prominent in the diagnostic possibilities, because the intestinal tract is so much less frequently the site of malignant disease. Furthermore, in the long distance between the pylorus and the anus certain parts are much more susceptible than others to cancer, so that within the intestinal tract the part to which the symptoms point again helps us to determine the probability that cancer exists. About this probability of cancer in different parts of the intestine, as well as about the evidence that speaks for the disease in each part, one must think very carefully if an early accurate diagnosis is to be made, for only early diagnosis makes surgical cure a probability.

A. CANCER OF THE DUODENUM. This is a very rare site for malignant disease. Nevertheless, the symptoms produced when the disease does occur are so striking that the interpretation ought to be easy. Like cancer elsewhere in the body, the growth here produces such general manifestations as anemia and cachexia, pain and often a palpable tumor; the pain and tumor are usually located in the upper right quadrant of the abdomen, more accurately in the right hypochondrium and epigastrium. In addition, certain special symptoms arise, according to the part of the duodenum involved. Boas classifies duodenal growths with reference to the biliary papilla into three varieties: (1) Suprapapillary, (2) circumpapillary (3) infrapapillary.

1. In *suprapapillary* cancer, no localizing symptoms arise until stenosis of the bowel results. As soon as stenosis occurs, the symp-

<sup>1</sup> Read at a meeting of the Nevada State Medical Society, at Goldfield, Nevada, October 5, 1909.

toms and signs become those of stenosis of the pylorus, with dilated stomach, and it is usually impossible to decide clinically whether the cancer originated at the pylorus or below it. In such a case—with general symptoms of cancer, such as anemia, cachexia, and loss of weight; with localizing symptoms, such as pain and a palpable tumor in the right hypochondrium; with special symptoms, such as food retention and repeated vomiting of stagnating contents; and the physical signs of dilated stomach, such as tumor, peristaltic wave, succussion splash and the proof of food retention by the stomach tube—a diagnosis of cancer at the pylorus would almost certainly be made, and in most instances it would be correct, because of the much greater frequency of cancer there than in the suprapapillary portion of the duodenum.

2. *Circumpapillary* cancer furnishes a new and prominent symptom—jaundice; with anemia, cachexia, and loss of weight as before; tumor in the right hypochondrium; but less pain as a rule and less of the former gastric manifestations. Jaundice is progressive and ultimately profound; and the symptoms characteristic of this condition become the predominant ones. Differentiation from malignant disease originating in the common duct, or in the head of the pancreas, or in the lower portion of the liver, would in such a case be practically impossible. Minute points of difference can be cited, but speaking from the view-point of these other conditions, the distinguishing marks are of little real value.

3. *Infrapapillary* cancer introduces still other characteristic symptoms and signs into the clinical picture. Stenosis of the duodenum below the papilla leads to stasis of the bile and pancreatic juice, their regurgitation into the stomach and their rejection from the body by vomiting. There is a large epigastric distention due to dilatation not only of the stomach but of the duodenum above the point of obstruction; copious vomiting of dark brown material resembling bile, neutral or alkaline in reaction and responding to chemical tests for bile; the presence in the fasting stomach in the morning of quantities of this same fluid, even though the organ has been carefully washed out the night before; and stools that are white and lacking in bile. This combination of symptoms and signs corresponds to no other condition exactly, though it resembles most closely acute dilatation of the stomach, and at first may be mistaken for it. The persistence of the symptoms; the development of a tumor in the epigastrium; the absence of bile from the stools; and the occurrence of increasing cachexia and malnutrition should serve to identify the case as one of duodenal cancer.

After all, two facts afford us consolation when we consider the difficulties and uncertainties of diagnosis in duodenal cancer; (1) that cancer in this part of the bowel is extremely rare; and (2) that all the conditions resembling it closely and causing the confusion in decision, demand operation for relief, and no fatal mistake can be made by advising surgical intervention when in doubt.

B. CANCER OF THE JEJUNUM AND ILEUM. According to all observers, cancer is rare in the ileum and still more rare in the jejunum. The whole of the small intestine seems singularly exempt from attack, as compared with the stomach above and the colon and rectum below. It is fortunate that this is so, for the jejunum and ileum particularly are difficult of investigation and their ailments hidden from observation. Cancer in this part of the bowel, as elsewhere, causes anemia, cachexia, and malnutrition; with localizing symptoms, such as attacks of colic, alternating constipation, and diarrhoea, sometimes hemorrhages, but nothing to point to the small intestine rather than the large as the site of the disease. Even when a tumor is palpable, as it most often is not, we have no positive way of determining its site. But in such a discouraging condition of affairs it again is a comfort to reflect that cancer in the small intestine, at least below the duodenum, is almost never found, not only by the clinician, but also by the surgeon and the pathologist.

C. CANCER OF THE COLON. Beyond the ileocecal valve the incidence of cancer rapidly increases, and we come into the presence of a lesion fairly common. To prove that this is not merely an individual experience, the statistics collected by Brill<sup>2</sup> are convincing, for he found that out of 3,563 cases of intestinal cancer reported by various observers, only 89, or 2.5 per cent., were in the small intestine. Nothnagel<sup>3</sup> records that out of 343 cases of carcinoma of the intestine discovered during twenty-four years among the autopsy material of the Pathological Institute of the General Hospital in Vienna, only 17 were in the small intestine—less than 5 per cent. In the investigation of any case suspected to be intestinal cancer, we start, therefore, with the probabilities all against a growth above the ileocecal valve. As with all diagnosis, our data here are obtained from two sources—subjective and objective evidence—the patient's story and our own observations.

I. THE SUBJECTIVE EVIDENCE. The clinical history of cancer of the colon is based largely upon increasing obstruction of the bowel caused by the growth; and the symptoms are mainly those of stenosis. The three complaints most often heard are of increasing constipation, flatulent distention, and recurring attacks of colic. Each of these is of great importance, but none alone is sufficient to cause more than suspicion; while even the coincidence of all three does not afford certainty without the other data furnished by various methods of examination.

1. *Increasing Constipation.* This is usually the first symptom to attract the patient's attention. Previously regular about daily defecation, he gradually comes to require the aid of laxatives; these gradually fail to act; the constipation grows more and more

<sup>2</sup> AMER. JOUR. MED. SCI., 1904, cxxviii, 824.

<sup>3</sup> Diseases of the Intestines and Peritoneum, Nothnagel's Encyclopedia, p. 413.

obstinate; the patient finds the greatest difficulty about getting the bowels to move at all; and at last there occurs complete occlusion. The following case illustrates this very common history:

CASE I.—A man, aged fifty-six years, was seen in June, 1907. His chief complaint was obstinate constipation. This had begun five or six years before, gradually increased in severity, and had been worse for the last year than ever. For six months he did not have a voluntary passage, and had taken all sorts and kinds of physic in increasing doses, more and more being required to produce any effect. Recently he had become "run down," weak, easily tired by exertion, and had lost ten pounds in weight. He had no pain until the last month before he sought advice, but during that time recurring attacks of what he called "the gripes." Over the left side of the abdomen, in the course of the descending colon, there were found numerous discrete lumps, movable and not tender, evidently retained feces. No other tumor was palpable. Operation revealed a malignant growth involving the sigmoid flexure and descending colon, hard and firmly adherent, too extensive for removal. The patient died a few months later.

2. *Flatulent Distention.* This by itself is by no means a sign of cancer of the colon. In fact, it more often means something else. When persistent, it almost invariably means the retention of fecal masses in the colon, and disappears most certainly after a brisk purge. The danger is that the diagnosis will not go beyond this fecal retention, and that the cause of it will be overlooked, particularly if chronic constipation is associated, this apparently explaining both the fecal accumulation and the flatulent distention. The following case shows how flatulence may be practically the only symptom and how cancer of the colon may for months give little other sign of its presence.

CASE II.—A man, aged sixty-two years, first consulted me in December, 1906, complaining that he awakened every morning early with a feeling of distention and tightness in his abdomen. This so annoyed him that he always had to rise and stir about; but as soon as his bowels moved, and gas was passed freely, he had no further trouble during the day. This difficulty had been going on every morning for months. Otherwise he felt well, and had no complaint to make. He was a very large, rather corpulent man, florid and apparently in perfect health. There had been no loss of weight. The abdominal examination, repeatedly made, was always negative as regards tumor or tenderness, but the bowels were always found distended with gas. They moved regularly every day, and various laxatives advised only caused diarrhoea and cramps, but did not prevent the flatulent distention. Finally, in April, 1907, after taking castor oil one evening, violent pains were set up, and continued all night. The next morning the abdomen was found greatly distended, rigid, and tender; the pulse rapidly grew irregular and weak, and in a few hours the patient died. Autopsy showed a rent in the ascending

colon near the hepatic flexure, with escape of a large quantity of feces into the peritoneal cavity, and a nodular carcinomatous constriction, annular, hard, and practically occluding the lumen, just beyond the rent.

3. *Recurring Attacks of Colic.* These do not always occur. When they do, they are usually associated with alternating constipation and diarrhoea. The bowels for a time are very obstinate and refuse to respond to laxatives; then comes a sharp attack of colic, with diarrhoea and profuse discharges. This is followed by another period of constipation, terminating sooner or later in colic and diarrhoea. In the interval between attacks there is usually no pain at all. Such a history does not necessarily mean cancer of the colon, but it does mean stenosis of the large bowel, fecal accumulation, increased peristalsis due to mechanical irritation, and emptying of the retained contents. Ultimately the time arrives when the stenosis cannot be overcome by these more violent waves of colicky peristalsis, and complete intestinal obstruction occurs, and possibly rupture of the bowel, as in the case last reported.

4. Finally, certain symptoms expected in the clinical history of cancer elsewhere must not be looked for in cancer of the colon until very late, and their absence must not mislead. There is usually no loss of weight in consequence, and nutrition is but little disturbed. The patient does not complain of weakness or exhaustion. There may be no noticeable anemia or cachexia, and the appearance continues to be that of health. Pain is usually absent, except during the attacks of colic. In fact, before the development of marked mechanical interference with the lumen of the bowel, cancer of the colon gives little sign of its presence, and it is not until late in its history, when metastases to other organs have already occurred, and operative interference is practically useless, that the disease is usually discovered.

II. THE OBJECTIVE EVIDENCE. This includes all that can be found out about cancer of the colon by various methods of examination. These methods comprise physical examination of the abdomen, examination with the x-rays, and examination of the feces and of the blood.

1. *Physical Examination of the Abdomen.* The whole object of this is to discover whether or not a tumor is palpable, and if it is found, to ascertain whether it is really a growth arising from the colon. (a) When no tumor is found, the diagnosis of cancer of the colon nevertheless cannot be set aside, for the annular carcinoma, encircling the bowel with a ring of hard, sclerotic tissue, may be absolutely incapable of detection by palpation through the abdominal wall, particularly if the wall is thick with fat or if the intestines are constantly distended by gas, as in Case II. Or, the tumor may be so situated that it is inaccessible for palpation, as beneath the liver or other intestinal coils. But repeated attempts should be made to

discover a tumor, before a decision is reached that it does not exist, and under special conditions, as well as under ordinary ones—for instance, after free purgation with castor oil and fasting for twenty-four hours, or in a hot bath to relax the abdominal walls, or under anesthesia. (b) When a tumor is found, there are no characteristics that positively identify it as connected with the colon. In size, it may be very small or very large. In consistence, it is usually very hard and cartilaginous, but so are cancerous growths within the abdomen arising from other organs. In form, it may be irregular and nodular, or rounded and smooth. In sensitiveness, it is usually tender to pressure, and may be extremely so; but, on the other hand, it may be handled without causing any pain at all. In mobility, it usually can be freely carried about within the abdomen by the examining hand; but if adhesions have formed, fastening the tumor to some adjacent organ or to the abdominal wall, it becomes quite fixed, and immobility of a tumor, therefore, does not negative the diagnosis of cancer of the colon. As regards position, it may be found in any part of the abdomen.

In the absence of any distinguishing characteristic on palpation, to assure the diagnosis of cancer of the colon, other means of physical examination must be employed for identification and other possibilities must be eliminated. The colon should be inflated with air, to determine the relation of the tumor to the bowel. Castor oil and high enemas should be employed to prove that the tumor is not fecal. The stomach should be inflated, and a test meal given to learn whether the tumor is possibly gastric. The kidneys should be catheterized if the slightest doubt exists as to whether the tumor is renal. A blood count will help to prove that the tumor is not splenic. Percussion and palpation with the patient in different positions will usually show when the tumor is hepatic—such as a Riedel's lobe. Finally, the employment of the other methods of diagnosis, presently to be described for cancer of the colon, will greatly aid in the identification.

As an instance, however, of the possibilities for error when a tumor is found, the following case is significant:

CASE III.—A woman, aged forty-five years, was seen in consultation in October, 1900, on account of dragging pain in the right side of the abdomen and back; she had lost slightly in weight, was constipated, and had symptoms of dyspepsia. In the right upper abdomen a tumor was found, corresponding in size, shape, and location to a prolapsed kidney. She was examined during her illness by seven different physicians and surgeons, who all agreed that she had a prolapsed kidney, the only question being whether the kidney was likewise diseased. It was finally decided that the organ was tuberculous, mainly on the testimony of a pathologist who claimed to have found tubercle bacilli in the urine, and that, therefore, the kidney should be removed. At the operation it was found that the

tumor was a cancer of the ascending colon, and that the kidney was in normal position and perfectly sound. The growth was removed, but the patient died a few months later from recurrence.

2. *Examination by the X-rays.* When this method of diagnosis has been desired, I have always referred my cases to someone expert in its use, for the making of the plates and for the interpretation of their meaning. I have, therefore, asked my associate, Dr. Charles M. Cooper, who has charge of the x-ray department at Lane Hospital, and whose experience is very large, to outline the method and its value in cancer of the colon. He writes as follows: "In the early diagnosis of cancer of the colon the x-rays are of little or no assistance. It is only after obstructive symptoms have developed that we can hope to show the delay point in the passage of the bismuth meal. Even then the interpretation is subject to fallacies, and must only be given special significance when in agreement with the clinical deductions. The demonstration of the nature of the obstructive agent presents still more difficulties. It is probable, however, that a comparison of radiograms of the bismuth-containing colon and of the air-filled colon will be of assistance in the field of diagnosis. Regarding the methods employed, there are three: (a) A bismuth test meal is administered by the mouth. This may consist of boiled rice, potato puree, barley broth, or minced meat, according to the desires of the patient. The amount for an adult is 400 grams by weight. One or two ounces of bismuth subcarbonate or oxychloride are rubbed up into a thin paste, with water or milk, and the food added little by little to the bismuth suspension, with which it is well mixed. The meal should be served warm. Normally, within six hours this has filled the cecum and the ascending colon. The whole colon is gradually filled, and twenty-four hours after the meal is taken the radiogram is made. (b) The bismuth may be given through the anus. Castor oil is administered the evening before and a cleansing enema the next morning. Then an enema is slowly introduced, consisting of a pint of mucilage of acacia to which one or two ounces of bismuth subcarbonate or oxychloride has been added. The tube should be of big bore, and it is only necessary to introduce it just past the anal canal. The bag containing the enema should not be more than one foot above the level of the buttocks. The patient rests on the back for forty-five minutes, and then the radiogram is made. (c) Examination may be made without the bismuth. If the bowels have been thoroughly evacuated, and the colon be partially distended with air through the rectum, radiograms can be obtained which outline very distinctly the ascending and descending colon. The sacculations and the separating folds may be very clear. The transverse colon does not lend itself so well to this method of investigation. Interpreting the plates obtained by any method, the points to be studied are: the extent of colon occupied by the bismuth mixture; the position of the colon; the uniformity of the



bismuth shadow; and the relationship of the colon to the other intra-abdominal organs."

3. *Examination of the Feces.* This no longer means simply an inspection of the bowel discharges, with reference to possible peculiarity in contour, such as flattened, ribbon-shaped, or pencil-shaped stools. These are significant of stenosis if they are found, but the stools may be normal in appearance, even with a large growth. Of more importance is the examination for mucus, pus, and blood. *Mucus* by itself is of little importance, for it is found in a great variety of intestinal conditions. *Pus* is of much more significance, but cannot be expected unless ulceration of the tumor has taken place. Even so, its presence means only ulceration of some kind, not necessarily cancerous; while its absence by no means negatives the diagnosis, for the growth may not have broken down. *Blood* may be found when no ulceration has occurred, from oozing or from traumatism by hardened feces, but it may be absent throughout the whole course of the disease. In any event, the amount is usually small and occult, mixed intimately with the feces. It is the combination of mucus, pus, and blood in the feces that is particularly significant. Persistence of this combination always means one of three things: cancer of the colon, dysenteric ulceration (especially amœbic), or an abscess that has ruptured into the bowels from some other viscus.

4. *Examination of the Blood.* The blood picture in cancer of the colon is that of a secondary anemia, with moderate leukocytosis, the differential count showing a relative increase of the polymorphonuclears. Naturally, no inference can be drawn from this evidence taken alone, but it is of value in connection with the other data, both for direct and differential diagnosis.

D. CANCER OF THE RECTUM. Malignant newgrowth originating in the sigmoid flexure or below is one of the most insidious diseases which we ever meet, and almost, as a rule, it has advanced beyond the stage of operability before it gives rise to symptom that lead the patient to seek advice. It does not cause anemia, cachexia, or loss of weight and strength until late in its history, and its local manifestations may be altogether overlooked for a long time. These local manifestations occur in several groups: (1) Those due to bowel obstruction; (2) those due to pressure on surrounding parts; and (3) those due to ulceration of the newgrowth. The symptoms arising from bowel stenosis are very much the same as those occurring when the growth is higher in the colon, namely, increasing constipation, flatulent distention, and paroxysms of pain. These complaints may be the only ones, as they were in the following case:

CASE IV.—A man, aged sixty-seven years, seen in October, 1908, complained that for three months he had been annoyed by increasing difficulty in getting his bowels to move. He had not much pain

except after cathartics were taken, but felt full of wind all the time, and bloated. His appetite was good, and he had not lost appreciably in weight. His abdomen was corpulent and its walls thick, so that palpation was difficult; but distinctly greater resistance and tenderness were found in the right lower quadrant than elsewhere. As no satisfactory evacuation of the bowels could be produced by cathartics or enemas, exploratory laparotomy was advised. This revealed a large, hard, inoperable carcinoma, filling the upper pelvis, apparently originating from the sigmoid flexure. The mass felt in the right lower quadrant, between the crest of the ilium and Poupart's ligament, was found to consist of enlarged retroperitoneal glands.

The symptoms in another case may be largely those from pressure of the growth upon surrounding parts. Pain in the region of the sacrum and the lower back, bladder irritation and tenesmus, or pain in the distribution of the sciatic nerve result. These symptoms may be added to those mentioned in the first group, and so serve to throw light upon the situation of the growth; or they may be the only ones of which complaint is made.

In still another group of cases the earliest manifestations are those due to ulceration, and in these the principal complaint is of chronic diarrhœa or bloody discharges, or both. Quite a common history is one of several loose passages each morning after rising, often with tenesmus, until the rectum is empty, and then no farther trouble until the following day. These passages consist of mucopurulent material mixed with the feces. With this history there is commonly complaint of increasing weakness and pallor, possibly of pain in the lower back and of urinary disturbance. Finally, the symptom that first alarms the patient may be the passage of bright red blood. Even then the condition is only too often assumed to be nothing but piles, until discovery of the true state of affairs comes too late. The following case shows what sort of history may be expected from this group:

CASE V.—A woman, aged seventy-five years, seen in September, 1907, stated that about five years previously she began to notice clots of blood in her bowel movements, and at times bright red blood. This had continued at intervals ever since. At the time she sought advice she was passing bright red blood every day; in fact, it came then even without bowel movements, and she had to wear a cloth all the time, even at night, because pus and blood ran constantly from the bowel. Besides this she had pain in the rectum now and then, but not constantly; a sense of pressure and fulness there most of the time, and particularly when at stool. The bowels were obstinately constipated, and when she took physic for relief, she had many passages, with great tenesmus and suffering. She had lost about fifty pounds in weight within the last two years. Rectal examination showed an irregular, hard growth about the size of a

turkey's egg, situated about three inches above the anus, with soft, necrotic edges around the lumen of the bowel. Operation was advised, but declined. Six months later I saw her again in consultation, when a large tumor mass almost completely filled the pelvis. She died soon afterward.

One of the curious facts about cancer of the colon and rectum is the early age at which it may occur. The following case is of special interest in this connection, as well as for its manifesting itself first by hemorrhage:

CASE VI.—A man, aged thirty years, seen in July, 1907, complained that for months previously he had noticed after stool that there would be a little bright red blood at the anus, but not constantly. But a few days before I saw him he had passed a large quantity of bright red blood, with some clots, and this gave relief to a pain he had previously been having in his back. Since then bleeding had persisted every day in greater or less quantity. He was a large, well-nourished man, and no abnormality whatever was found in the abdomen, except tenderness low down on the left side over the descending colon. Rectal examination showed a tumor filling up the bowel, situated mostly on the anterior wall, irregular in contour, about four inches from the anus. Operation was advised but refused. I saw him again, in consultation, in the following November. In the meantime he had been treated by a Chinese doctor until complete obstruction of the bowel occurred, then had been compelled to seek the advice of a surgeon, who did a left inguinal colostomy. At this second examination he was found to have a large tumor practically filling the entire pelvis—tender, irregular, nodular, with bloody, purulent discharge—and had become greatly emaciated and weakened. A portion of the growth removed for pathological examination was shown to be carcinoma.

As aids to diagnosis in cancer of the rectum there are all those mentioned for cancer of the colon; but there is one other available here that was not available there, namely, rectal examination. In rectal carcinoma, abdominal examination may show no abnormality whatever, until such time as a very large tumor has developed, or masses of enlarged glands present themselves, or the liver is involved by metastasis, or ascites has occurred from general peritoneal carcinosis. For a long time the most careful abdominal palpation may reveal no tumor, because it is hidden below the brim of the pelvis; but during all this time examination through the anus will at once reveal the tumor's presence. This examination should be first by digital palpation; or if this is negative, then the cylindrical rectal speculum should be used and the parts inspected, as can be done with the sigmoidoscope even as high as ten or twelve inches from the anus. The routine rectal examination in every case of chronic digestive disturbance will often save the diagnostician from grievous error as well as the patient from fatal delay, until his case is beyond

surgical aid. This suggestion of rectal examination as a regular part of the investigation, whether symptoms seem to call for it or not, is by no means a new idea; yet the procedure is constantly forgotten: A careful clinical history should always be obtained; examination of the abdomen in every part should never be omitted; x-ray plates after bismuth injections should be remembered in all obscure cases; the discharges from the bowel should be examined not only by gross inspection, but also chemically and by the microscope; and the complete blood count should be made by an expert. But all these means of reaching a diagnosis may fail to reveal the existence of cancer of the rectum, when simple rectal examination would have shown its presence at once.

In conclusion, I repeat the sentences with which this paper began: that in considering the cause of any chronic digestive disorder, cancer can never be left entirely out of account, and can never be eliminated from the calculation until after all the evidence has been obtained and carefully weighed. To this conviction I would add one other, that no examination for any chronic digestive disorder is complete until a rectal examination has been made.

## THE ROUTINE EXAMINATION OF THE ŒSOPHAGUS.

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UNTIL comparatively recently an analysis of the symptomatology and an examination of the œsophagus with sounds of divers make and form exhausted our means of investigating this tube. The association of the knowledge so acquired, with the postmortem findings, has led to the establishment of certain fundamental facts, an acquaintance with which is essential prior to our investigation.

From such we cull the following:

1. Difficulty of swallowing is the overwhelmingly important symptom indicative of a lesion of, or interference with, the œsophageal tube.

2. Of every 100 patients who come complaining of this symptom, from 60 to 90 suffer from malignant disease. This comprises from 5 to 6 per cent. of all carcinomas. Of persons so afflicted, over 70 per cent. are males. This raises the question whether syphilis does not play as important a role in the etiology of cancer of the œsophagus as it is now believed to play in cancer of the tongue. Of these carcinomas, 10 per cent. arise in the cervical region, 40 per cent. at the bifurcation of the trachea, 30 per cent. at the lower end, while the remaining 20 per cent. are really instances

of gastric carcinoma which have led to œsophageal symptoms. Of the 10 cases which I have seen, 5 occurred at the tracheal bifurcation, 1 in the neck, 2 at the lower end, while 2 were of gastric origin.

3. In interference with deglutition from causes outside the œsophagus, difficulty of swallowing is rarely the first or only complaint, as it not uncommonly is in diseases of the tube itself.

4. The œsophagus is relatively insensitive and therefore severe pain is infrequent in lesions confined to its walls. The acute rending pain, retrosternal, of short duration, which most individuals have experienced on gulping down too quickly too large a swallow of fluid, and which appears to be due to an acute stretching of a segment of the œsophagus, is obviated by the slow method of taking food which these patients quickly learn to practise. Head states that the œsophagus is segmentally connected mainly with the fifth dorsal segment, and that the two maxima brought out by passing a bougie are to be found (*a*) at a spot two inches from the middle line posteriorly at the level of the angle of the scapula, and (*b*) at a spot in the fifth interspace anteriorly about half an inch internal to the nipple line. Skin sensitiveness may be associated with these pains, and overflow into the neighboring dorsal and into the cervical segments may occur. It is only during exacerbations or after the passing of instruments, in my experience, that we can outline these areas and skin segments, and we may conclude that severe pain commonly implies a spread of the disease beyond the œsophageal wall.

5. The œsophagus is not provided with location nerve terminals, and consequently the patients' fixed ideas relative to the seat of the lesion are absolutely untrustworthy. The non-appreciation of this fact has led to errors of localization. Particularly apt is he, no matter where the real lesion, to insist that the delay occurs just above the jugular fossa, as he there feels a choking sensation, perhaps because near this locality the striped constrictor muscles become continuous with the non-striped muscle of the œsophageal wall.

6. Auscultation of the œsophagus as a diagnostic method gives meagre information. As Hertz points out, the factors concerned in the production of the first and second sounds have been probably misinterpreted. The whole subject will bear re-investigation, and meanwhile conclusions drawn from its findings are unreliable. The gurgling murmur clearly audible without auscultating should probably be excepted.

7. Grave organic disease of the œsophagus frequently leads to disturbed innervation of the tube. The clinician who is unaware of this source of error may mistake the complication for the real lesion, and so incorrectly diagnose both the locality and the nature of the disease. I have seen this occur.

8. The amount of dilatation that takes place above a carcino-

matous stricture is relatively small, and the regurgitation of a large quantity (above three ounces) of food from the œsophagus should suggest a cause other than carcinoma. Very little dependence, as I have repeatedly noted, can be placed upon the patient's estimation of the amount he regurgitates. This must be seen and measured. Since free hydrochloric acid is often not to be found in the stomach contents of patients afflicted with œsophageal carcinoma, its absence from the regurgitated food does not prove the latter to come from the œsophagus. The excessive mucous secretion and the unswallowed saliva frequently lead the patient to believe that he regurgitates more food than he actually does.

9. Emaciation to an extreme degree may ensue when swallowing is seriously impaired, though the lesion be non-malignant.

10. Unilateral paralysis of the vocal cord is quite a common occurrence during the course of a carcinoma of the œsophagus. This may be present in the absence of any change of voice.

11. The act of swallowing is reflexly initiated by the contact of the food with the mucous membrane of the posterior portion of the tongue and the fauces. The food is thrown back into the required position by the voluntary elevation of the fore part of the tongue and the contraction of the mylohyoid muscles. In one patient with difficulty in swallowing, whom I was asked to see, this necessary preliminary manœuvre was found to be impossible, and the bismuth capsule lay motionless in the fore part of his mouth. When the bolus has reached the back part of the tongue it is no longer under control, and the involuntary reflex stage of deglutition begins. The peristaltic wave so induced can pass over any muscular block whether caused by lesion, ligature, or section. The loss of the swallowing reflex is clinically indicative of a bilateral lesion, as either both superior laryngeal or both recurrent laryngeal nerves must be paralyzed to prevent the occurrence of deglutition.

The special importance of a full and correct history in this field of work must always be kept in mind. In some instances it is characteristic of the particular lesion from which the patient suffers. I would draw attention to two sources of error: (*a*) Since carcinomas frequently develop on the site of old lesions or in the course of other chronic diseases, such as cirrhosis of the liver, the immediate trouble may be regarded as having been of much longer duration than is actually the case, and so an unduly favorable diagnosis made. (*b*) Carcinoma of the œsophagus is an incurable disease. The patients receiving little help, visit many physicians. Some have argued with them the reasons for the different diagnostic possibilities. The patients desirous of believing that they suffer from the least serious malady will narrate to a physician whom they later see a history strangely at variance with the real facts.

THE CLINICAL EXAMINATION. It may seem trite to emphasize the fact that a thorough clinical examination should always precede

all the special methods of investigation. Nevertheless, so frequently is this left undone in private practice, clinic, and hospital work, that it must be that in our teaching we have failed to inculcate sufficiently the value of a system in diagnostic work. Of special importance is it to emphasize this in diseases of the œsophagus, for many of the patients so afflicted first find their way into the surgical clinic, where the gullet sounds are always handier than the percussion finger or the stethoscope. With the dissemination of the knowledge of the diagnostic value of the x-rays and of the œsophagoscope, some patients will first visit the radiographer, whose clinical experience is commonly of a meagre character, and who, overconfident of his results, may wrongly interpret what he thinks he sees; other patients will seek the specialists in throat diseases, from whom, indeed, has come the impetus in œsophagoscopy work. They, little practised in the art of general clinical examination, will be often tempted to œsophagoscope these patients without first having them thoroughly investigated from the clinical standpoint. If this should occur, some aneurysms will be ruptured and perhaps some œsophageal walls perforated.

After the clinical examination we proceed to examine the larynx and pharynx with the laryngoscope. Any cord paralysis or laryngeal abnormality is noted. By assuming Killian's position we can look down the trachea. By carrying out the manoeuvre of von Eicken after cocainizing the larynx we can, without distressing the patient, examine the hypopharynx, that is, the part of the pharynx which lies below the aperture of the larynx. If nothing abnormal be evident, the patient massages his throat below this level in an upward direction, and I have seen the saliva which does not pass the stricture re-appear in the pharyngeal slit. In a certain percentage of cases a portion of the growth may be thus seen blocking the hypopharynx, and the physician will be saved the humiliation of unwittingly passing the œsophageal tube, or maybe food in the larynx. In some cases it is better to delay considering hypopharyngoscopy until after the radiographic investigation has been carried out. It may not then be necessary.

If our examination so far be negative, we watch our patient as he tries to swallow, first, a mouthful or two of fluid and later some bread. We note if the voluntary contraction of the mylohyoid muscles and the accompanying elevation of the larynx occur, and if the involuntary part of the deglutition act ensue. After the patient has swallowed as much food as he can, we note:

1. If there be any change in the shape of the neck; if by shaking the patient's throat we can produce a succussion murmur. This was readily obtained in one of the cases of œsophageal diverticulum and led to the recognition of the seat of the mischief. Or if, after giving the patient two or three bismuth capsules, they can be massaged from the lower part of the neck into the pharynx. This

was easy of accomplishment in another case of œsophageal diverticulum, and similarly led to the discovery of the diverticulum.

2. If the laryngeal picture has changed. In one patient the filled diverticulum so displaced the larynx that the cord ran from behind forward, and to the left instead of directly forward, as they did before the sac was filled.

3. If there be any change in the character of his radial pulse from that exhibited prior to his eating. In one patient whom I saw, and who had a diverticulum, the filled sac evidently compressed the big vessels, particularly during deep expiration. If the diverticulum be in the neck region, it is the carotid and jugular pulse that should be inspected.

The patient is now referred to the x-ray department before any bougie or metal tube is passed.

THE X-RAY EXAMINATION OF THE ŒSOPHAGUS. The normal œsophagus throws no shadow, and it is only after introducing within it some substance or object impermeable to the rays that we are able to locate their position and study their form and function. Even with this aid the shadow cast in the anteroposterior position by that portion of the œsophagus lying below the arch of the aorta is often indistinguishable from the shadows due to the vertebral column and the overlying descending thoracic aorta.

In the left posterior or right anterior positions, the dark shadows due to the vertebral column, on the one hand, and to the heart and aorta, on the other, are separated by a clearer area, which is termed the clear middle area. Through this field the normal œsophagus runs, and it is this area that we investigate. The supra-aortic portion of the œsophagus is best investigated in the anteroposterior position.

Most of the better known röntgenologists agree that fluoroscopy is the method of choice in the x-ray investigation of diseases of the œsophageal tube. Having followed this line of work as an aid to clinical diagnosis, rather than as a branch sufficient unto itself, while recognizing the high value in skilled hands of the screen, and especially of orthodiagraphic work, I believe:

1. That fluoroscopy is a procedure dangerous to the operator, and necessitates the expenditure of too much time to render its adoption likely for general clinical work.

2. That many clinicians are not prepared to accept reports emanating from the x-ray room which are not based upon shadows which can be registered on the photographic plate, and so at least be open to the inspection of the physician.

3. For teaching purposes it is necessary to register the abnormality if one desires sufficiently to impress the student with the value of this method of examination.

We proceed as follows:

1. If the previous examination leads us to suspect the presence of a supra-aortic œsophageal pouch, we ask the patient to swallow



two or three teaspoonfuls of a mixture made up of equal parts of bismuth subcarbonate or bismuth oxychloride and sugar of milk, to which sufficient water is added to give it a paste-like consistency. We then make a radiogram as of the lung apices, using the compression diaphragm, the lower edge of which rests on the manubrium sterni. Fig. 1 is of such a patient in whom this procedure was adopted. The bismuth-filled pouch is very evident. It is cleanly bordered and has no funnel-shaped opening running downward from its base, this serving to distinguish it radiographically from the local dilatations which may form immediately above œsophageal strictures.

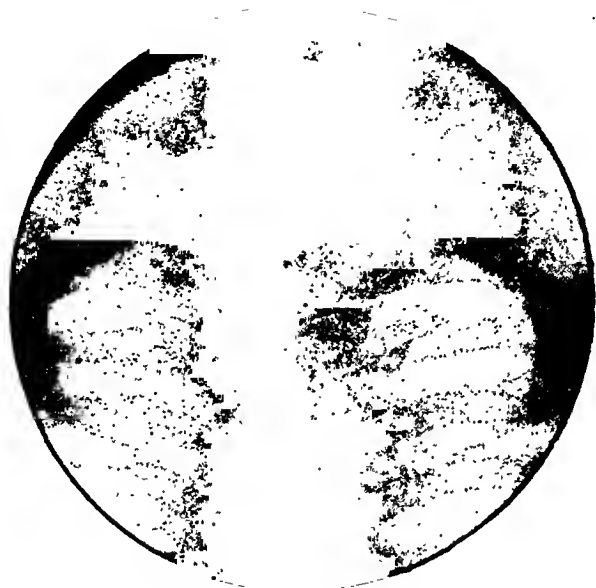
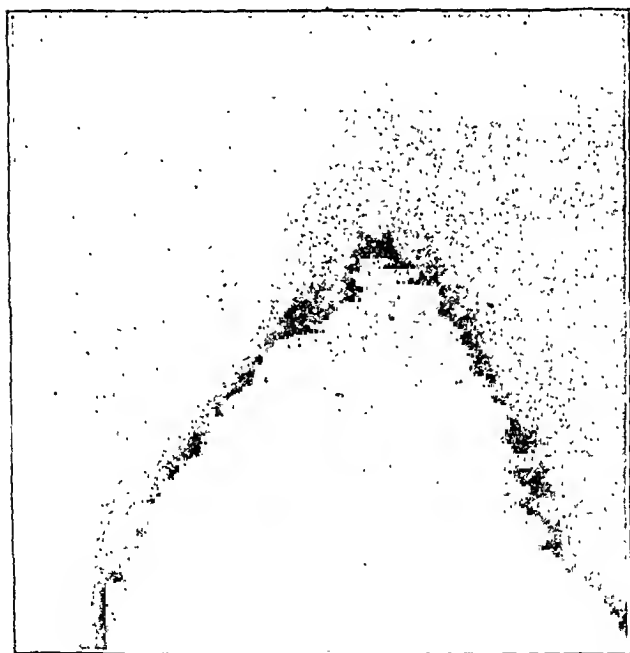
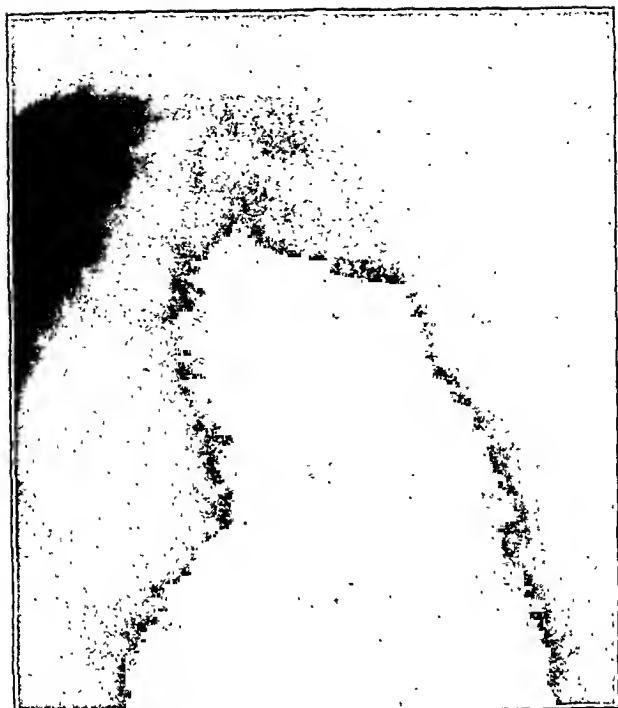


FIG. 1 is from a patient seen in consultation with Dr. Terry. The complaint was difficulty of swallowing. The clinical examination revealed a gurgling murmur on swallowing, and a succussion splash after drinking and shaking the neck. The radiogram was taken after bismuth paste had been swallowed. The diverticulum is very distinct. The marker is over the cricoid. The œsophagoscope showed an absence of ulceration or malignant change. The sac was later removed by Dr. Wallace I. Terry.

2. If we suspect the presence of a pouch lying below the level of the aortic arch, we administer bismuth paste, and then radiograph the patient in the right anterior oblique position. The pouch will show the same characteristics, but appears in the clear middle area, of which I have spoken.

3. If we suspect the presence of a spasmodic contraction of the cardia with an accompanying œsophageal dilatation, we ask the patient to drink as much as he can of a pint of koumiss with which an ounce of bismuth subcarbonate has been well mixed. The suspension is well shaken immediately prior to use. The patient is then at once radiographed in the right anterior oblique position.



FIGS. 2 and 3 are from a patient seen through the kindness of Dr. Kugeler. The original complaint was vomiting of considerable blood. The clinical findings were an alcoholic history, a large spleen, a small liver, and hemorrhoids. The diagnosis was cirrhosis of the liver. Later there was complaint of difficulty of swallowing. A clinical examination for a cause was negative. The sound was arrested at the cardia. The plates are explained in the text. Esophagoscopic examination was arranged for, but was not carried out, and later was considered inadvisable. Later, there was paralysis of the right vocal cord, coughing up of a cupful of pus, and death. The postmortem revealed carcinoma of the esophagus, as described; a peri-esophageal abscess which had ruptured into the bronchus and into the pericardial sac; cirrhosis of the liver.

The bismuth-containing œsophageal sac stands out very distinctly and may fill almost the whole of the clear middle area.

4. If we suspect the presence of a carcinoma of the œsophagus, we ask the patient to swallow a few teaspoonfuls of the bismuth paste and then one or two capsules each containing seven and one-half grains of bismuth subcarbonate. The patient is then radiographed in the right anterior oblique position.

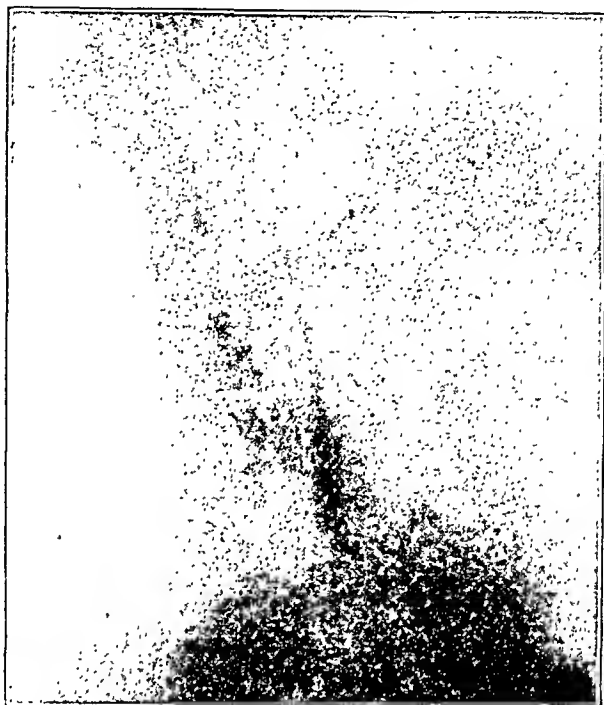


FIG. 4 is from a patient seen in consultation in whom a diagnosis of an œsophageal diverticulum had been made, being based upon a falsified history, the patient's invincible belief that the obstruction lay at the level of the jugular fossa, an occasional hindrance to the tube about this level, and a wrongly interpreted x-ray plate. The clinical examination showed great emaciation, no enlarged glands, no pupillary or laryngeal changes, no palpable stomach tumor, no systemic changes. Bismuth capsules were administered. With the fluoroscope one lost track of them in the upper part of the gullet. The bismuth, however, collected and became evident at the cardiac end of the œsophagus. The gelatin capsules evidently softened and allowed the bismuth to escape at the point where the bismuth streak begins. The œsophagoscopic examination showed a normal œsophagus. A probable diagnosis was made of spasmodic stricture of the cardia, dependent upon a malignant growth below. Operation was advised and performed. A large malignant growth infiltrating the stomach walls and situated up under the liver margin was found. Jejunostomy was done. Death occurred a week later. The postmortem revealed the œsophagus not involved in the growth.

Figs. 2 and 3 are of a patient who died from a carcinoma of the œsophagus. In Fig. 2 two bismuth-containing capsules are evident. They are arrested at the upper limit of the growth. In Fig. 3 the shadow cast by the bismuth paste is seen. The œsophageal lumen is alternately dilated and constricted, but the bismuth paste shadow is continuous. Postmortem the œsophageal wall from the

level of the tracheal bifurcation to the cardiac end was found to be involved, much of the growth, however, having ulcerated away. After these radiograms were taken a peri-œsophageal abscess formed and opened into the trachea and later into the pericardial cavity.

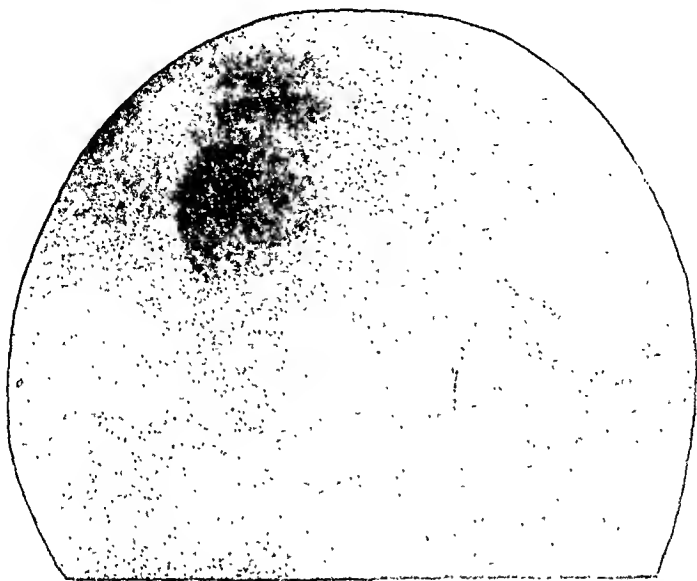


FIG. 5 is from a patient, aged sixty-five years. The complaint was shortness of breath of eight years' duration, difficulty in swallowing, and angina-like pains of a year's duration. The clinical examination gave evidence of the presence of general arteriosclerosis and of some bronchitis. A gurgling murmur was heard on swallowing. A succussion neck splash was produced after swallowing fluids. Laryngoscopy after swallowing bismuth paste showed a displacement of the vocal cords, as described. Hypopharyngoscopy was negative. The radiogram taken after swallowing bismuth paste shows the diverticulum filled with the bismuth mixture. The passage of the tubes was resisted at the cricoid, and regurgitation of food ensued. Œsophagoscopy showed a spasm of the œsophagus just below the pharyngeal slit, due to the presence of a little grayish slough, which had been probably produced by a previous œsophagoscopy (he had been previously œsophagoscoped twelve times, and no diagnosis arrived at); below that the mouth of a diverticulum, which was only evident when the sac was filled with bismuth paste; and below that in the upper thoracic portion of the œsophagus, a stricture with a curved semilunar opening situated at the side. This lower stricture is difficult of explanation, but further fluoroscopic and radiographic examination suggests that a mediastinitis involving the pericardium and the œsophagus is present in this patient. The patient is still under observation.

In other cases of carcinoma the plate shows a shadow similar to that thrown by the bismuth-filled diverticulum, but there is a funnel-shaped prolongation of the bismuth shadow through the stenosed area. Sometimes below the constriction the shadow broadens out again, there occurring a complicating spasm of the cardia, which temporarily delays the entrance into the stomach of the bismuth paste which has passed the stricture (see Fig. 6). Sometimes capsules are arrested at places past which the sound is found readily to glide, as in this case. When this occurs we suspect a paralysis of the muscular fibers of the œsophagus or perhaps their destruction, or an intermittent spasm.

5. If we suspect a narrow stricture, and wish to determine if there be a local dilatation above it, we can administer one of the capsules. This will block the opening. If the patient then swallows as much bismuth paste as he can, a radiogram will show the extent of the dilatation.

6. If the history and previous examination has rather suggested an extra-œsophageal cause for the difficulty of swallowing, or has led to no tentative diagnosis, we make two radiograms after the patient has taken the bismuth capsule and bismuth paste, one in the



FIG. 6 is from a patient aged fifty years. The complaint was difficulty in swallowing, of three months' duration. The clinical examination showed as positive findings a foetid odor to the breath, a dilated right pupil, an old right corneal scar, a secondary anemia, and a very slow method of eating; later, spitting up of blood. Laryngoscopic examination, etc., was negative. Bismuth paste and bismuth capsules were administered and a radiogram made. The print has been described in the text. The passing of sounds and œsophagoscope was deemed inadvisable until the former should be therapeutically required. A diagnosis of carcinoma of the œsophagus at the level of the tracheal bifurcation was made.

(NOTE.—If only bismuth paste were administered, and no spasm of the lower end of the œsophagus were present, a radiogram might give no evidence of the stricture.)

anteroposterior direction during suspended respiration, the plate to include the region of the neck; the other radiogram is made in the right anterior oblique position. One or both of these plates will show the seat of delay and give valuable information regarding the nature of the underlying lesion. If an aneurysm or mediastinal tumor be evidently present, they will show whether its position corresponds to the point at which the bismuth is delayed.

The further investigation, if any, depends upon the tentative conclusion that is formed after the association of the clinical and radiographic data:

1. If we conclude that an aneurysm is present, no further investigation is required or indeed justifiable.

2. If an aneurysm be present, but the location of the stricture be below the aneurysmal sac, no further investigation is justifiable, as the sac of the aneurysm might be ruptured.

3. If we are convinced that a carcinoma of the œsophagus is present, the less the instrumental meddling the better for the patient. The passage of instruments is only called for when their use is demanded for therapeutic purposes.



FIG. 7.—A capsule is seen lying behind the shadow due to the arch of the aorta. Bismuth paste and a large-bore stomach tube were passed without difficulty. A temporary retention of a capsule in this portion is not infrequent. Œsophagoscopy was considered inadvisable.

If further investigation be advisable, examination with the sound and the œsophagoscope is now in order. The passing of the sound should precede that of the œsophagoscope. Thus, we learn if the diameter of the gullet above the spot at which the capsule is arrested will allow of the passing of a tube of the diameter of the œsophagoscope.

The best bougies are probably those having a whalebone handle and interchangeable olive-shaped metallic heads of different sizes. They are neither too rigid nor too flexible. The method of use and the information they afford in cases of œsophageal carcinoma, œsophageal spasm, and stricture from extra-œsophageal causes other than aneurysm are well known and need no comment.

Œsophagoscopy is the last diagnostic means in this proposed scheme. It is a method often disagreeable to the patient, and if

done roughly or inopportunately, of considerable danger. Its employment demands a wise discretion and good sense on the part of the operator.

The technique of the examination is as follows:

1. The stomach should be empty, and the œsophagus, if dilated, should be washed out. No sound should have been passed for at least twenty-four hours.

2. An injection of  $\frac{1}{4}$  grain of morphine and  $\frac{1}{100}$  grain of atropine is given half an hour previously.

3. The structures of the throat are well anesthetized with a 10 per cent. solution of  $\beta$ -eucaine with adrenalin.

The patient may be examined in the sitting, left lateral, or dorsal position. I prefer, when possible, to have the patient seated on a cushion on the floor. The back and feet are placed against firm supports; another cushion is put under the knees. An assistant supports the head, which is dorsally flexed.

The patient is told to breathe quietly; to swallow when told to do so; to raise his hand if in pain, since he cannot speak; and to pay no attention to drooling saliva.

I use the Einhorn instrument, which carries its own light. I watch its passage over the back of the tongue past the epiglottis into the pharyngeal slit. The mandrin is then introduced and the instrument is carried past the inferior constrictor. The mandrin is then withdrawn and the further progress of the instrument watched. The previous investigation will have told us what bore instrument can be used and the length of instrument to be chosen. It is carried to the site of the lesion.

The appearance of the lesion is in many instances quite characteristic: the wrinkled sac of a diverticulum, the rosette-like appearance occasioned by a local spasm, the bleeding ulcerated nodules of a carcinoma if seen are readily recognized. In other instances the picture presented by extra-œsophageal growths is exactly similar to that seen in some cases of carcinoma.

The object of this paper, however, is not to describe the correct technique of, or the information gained by, hypopharyngoscopy, probing with sounds, and œsophagoscopy, and I have purposely refrained from speaking of double sounds and apparatus for determining the intra-œsophageal pressure. Rather it is threefold:

1. To record how simply one can often clinically gain serviceable information in cases of œsophageal diverticulum.

2. To show that radiography can be of considerable service in the investigation of these patients.

3. To advocate the adoption of the above outlined system in the investigation of patients afflicted with difficulties of deglutition. It will, I believe, prevent some deaths and will undoubtedly save much distress to a class of patients who already suffer much. Its advantage for teaching purposes is obvious.

## THE GASTRIC SECRETION.

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PERHAPS no one field in physiological or pathological chemistry contains more of interest than the results of a systematic investigation of the gastric secretion. This paper is based on a study of the vomitus from 81 patients, mostly derived from postanesthetic vomiting. No food particles were present in any of the specimens, for in Mount Sinai Hospital, as in other institutions, food and water are withheld for several hours before the patient is anesthetized. The results, as one can see from the tables, are of some interest and at some variance with opinions held by other observers.

Taking up the first of the columns, we find that the amounts vary from 20 c.c. to 240 c.c. This variance unquestionably is an individual one dependent on the length of the anesthesia, thereby influencing the amount of mucus swallowed, the watery element acting as a chemical stimulant; the psychical effect of both operation and anesthesia, the nervous temperament, etc., of the patient, all or each of which may influence the amount of gastric secretion. Larger amounts of gastric secretion may also be due to an existing functional condition or to a transudation following an abnormal resorptive power. Normally the fasting stomach may contain 10 to 20 c.c. of fluid.

The color question was also of interest: it was brown in 22, green in 37, colorless in 6, yellow in 7, gray in 8. Very few were perfectly clear, mostly all being turbid from the mucus present. Of the 37 green specimens, only 32 contained bile, thus confirming the opinion that not every green stomach contents is caused by the presence of bile. Mucus in various amounts is also influenced by some of the causes which tend to increase the amount of gastric secretion. It may be caused by mouth lesions—stomatitis, ptialism, pharyngitis, etc.—or by a catarrhal gastritis. Normally, there is always a little mucus present. In 6 there was no mucus, little in 37, moderate in 13, and much in 25.

The normal chemical reaction of the gastric secretion is acid, due to the presence of free acid, partly to acid salts (monophosphates), and partly to both. In the 81 specimens, 66 were acid to litmus, 9 were alkaline, and 5 were neutral.

The Congo paper reaction was positive in but 27 and negative in 53. This reaction is very generally used to determine the presence of free acids, and one is somewhat struck by the fact that 66 of the specimens were acid to litmus and but 27 of these positive to Congo, assuming that the gastric acidity is due to the free acids present.



TABLE I.

Case No.	Diagnosis.	Amount c.c.	Color.	Mucus.	Reaction.	Congo.	Bile.	Total nitrogen per cent.	Ammonia per cent.	Chlorine per cent.
1	Colporrhaphy	32	....	None	...	.....	Negative	0.168	0.018	0.231
2	Carcinoma of kidney	95	Brown	None	Acid	Negative	Negative	0.147	0.008	0.277
3	Endometritis	120	Yellow	Little	Acid	Negative	Positive	0.104	0.017	0.422
4	?	22	Yellow	Little	Neutral	Negative	Negative	0.073	0.0017	0.177
5	Pregnancy	31	Green	Little	Acid	Negative	Positive	....	0.015	0.419
6	Abortion	29	Brown	Little	Acid	Negative	Positive	0.148	0.015	0.397
7	Diseased appendages	88	Brown	Little	Acid	Positive	Negative	0.241	0.029	0.500
8	Renal colic	29	Colorless	Little	Alkaline	Negative	Negative	0.133	0.0204	0.256
9	Tumor of colon	65	Brown	Little	Acid	Positive	Positive	0.172	0.0204	0.497
10	Hemorrhoids	38	Brown	Much	Acid	Negative	Negative	0.246	0.035	0.532
11	Chronic nephritis	68	Brown	Little	Acid	Positive	Negative	0.199	0.029	0.536
12	Hemorrhoids	28	Green	Little	Acid	Negative	Positive	0.256	....	0.653
13	Ectopic gestation	94	Brown	Little	Alkaline	Negative	Negative	0.133	....	0.266
14	Carcinoma of rectum	50	Colorless	Much	Acid	Negative	Positive	0.014	0.030	0.401
15	Hernia	45	Colorless	Much	Acid	Negative	Positive	0.165	0.027	0.348
16	Appendicitis	46	Yellow	None	Alkaline	Negative	Positive	0.095	0.058	0.358
17	Cholelithiasis	102	Yellow	Little	Neutral	Negative	Negative	0.035	0.006	0.099
18	?	90	Colorless	Much	Acid	Negative	Positive	0.143	....	0.419
19	Appendicitis	25	Brown	None	Alkaline	Negative	Positive	0.201	0.054	0.398
20	?	60	Brown	None	Acid	Positive	Negative	0.145	....	0.344
21	Cholecystectomy	50	Green	Little	Acid	Positive	Positive	0.090	0.024	0.440
22	?	240	Gray	None	Neutral	Negative	Positive	0.123	0.036	0.277
23	?	150	Green	Little	Acid	Positive	Positive	0.070	0.027	0.270
24	?	64	Brown	Little	Acid	Positive	Negative	0.160	0.030	0.866
25	Appendicitis	60	Brown	Small	Acid	Positive	Negative	0.140	0.023	0.472
26	Ventral hernia	90	Green	Much	Acid	Negative	Positive	0.154	0.014	0.284
27	Hematoma	22	Green	Much	Acid	Negative	Positive	0.132	....	0.341
28	Appendicitis	77	Green	Moderate	Acid	Negative	Positive	0.199	0.018	0.124
29	Carcinoma of rectum	72	Green	Much	Acid	Negative	Positive	0.238	0.034	0.479
30	Appendicitis	67	Green	Much	Acid	Negative	Positive	0.126	0.017	0.238
31	Appendicitis	30	Green	Much	Acid	Negative	Positive	0.126	....	0.312
32	Glands of neck	53	Brown	Moderate	Acid	Positive	Positive	0.157	0.022	0.415
33	Nephropexy	32	Green	Moderate	Acid	Negative	Positive	0.104	0.010	0.405
34	Appendicitis	160	Green	Much	Acid	Negative	Positive	0.104	0.017	0.287
35	Tumor of breast	45	Green	Much	Acid	Positive	Positive	0.115	0.019	0.394
36	Appendicitis	36	Green	Little	Neutral	Negative	Positive	0.132	0.046	0.373
37	Carcinoma of rectum	67	Brown	Little	Acid	Positive	Positive	0.168	0.025	0.465
38	Salpingo-oophorectomy	28	Green	Little	Acid	Negative	Negative	0.081	0.007	0.145
39	Appendicitis	80	Brown	Much	Acid	Positive	Negative	0.036	0.012	0.433
40	Appendicitis	21	Green	Little	Acid	Positive	Positive	0.056	....	0.298
41	Gall-bladder	20	Brown	Little	Acid	Positive	Negative	0.362	....	0.454
42	Appendicitis	65	Green	Moderate	Acid	Negative	Positive	0.082	0.019	0.252
43	Tuberculous glands	52	Green	Moderate	Acid	Negative	Positive	0.244	0.034	0.366
44	Hernia	32	Colorless	Little	Acid	Negative	Positive	0.120	0.003	0.383
45	Appendicitis	78	Green	Much	Acid	Negative	Positive	0.210	0.012	0.273
46	Hernia	124	Green	Moderate	Acid	Negative	Positive	0.178	0.020	0.398
47	Ovarian cyst	68	Green	Much	Acid	Positive	Negative	0.193	0.019	0.383
48	Gastrostomy	65	Brown	Little	Acid	Negative	Positive	0.134	0.012	0.128
49	Appendicitis	85	Gray	Little	Acid	Negative	Positive	0.087	0.017	0.145
50	Appendicitis	95	Green	Mucus	Acid	Positive	Positive	0.154	0.018	0.348
51	Glands of neck	45	Brown	Little	Acid	Negative	Negative	0.224	0.039	0.539
52	Gall-bladder	140	Green	Much	Acid	Negative	Positive	0.120	0.025	0.351
53	Appendicitis	43	Green	Little	Acid	Positive	Positive	0.145	0.023	0.532
54	Appendicitis	40	Gray	Moderate	Alkaline	Negative	Positive	0.249	0.044	0.490
55	Fistula-in-ano	30	Yellow	Moderate	Acid	Negative	Positive	0.134	....	0.131
56	Varicose veins	36	Gray	Little	Alkaline	Negative	Positive	0.210	0.017	0.436

TABLE I—Continued.

Case No.	Diagnosis.	Amount c.c.	Color.	Mucus.	Reaction.	Congo.	Bile.	Total nitrogen per cent.	Ammonia per cent.	Chlorine per cent.
57	Abdominal cyst	34	Green	Much	Acid	Positive	Negative	0.098	0.041	0.571
58	Hernia	51	Green	Little	Acid	Positive	Positive	0.176	0.019	0.678
59	Appendicitis	25	Green	Much	Acid	Negative	Positive	0.087	....	0.224
60	Appendicitis	75	Green	Little	Alkaline	Negative	Positive	0.143	0.014	0.366
61	Tumor of breast	50	Green	Little	Alkaline	Negative	Positive	0.143	0.020	0.327
62	Appendicitis	90	Brown	Little	Acid	Positive	Positive	0.263	0.029	0.437
63	Appendicitis	60	Colorless	Moderate	Acid	Positive	Positive	0.148	0.015	0.408
64	Appendicitis	40	Green	Much	Acid	Negative	Positive	0.109	0.017	0.412
65	Salpingo-oöphorectomy	50	Brown	Moderate	Acid	Positive	Positive	0.146	0.015	0.344
66	Appendicitis	60	Green	Little	Acid	Negative	Positive	0.140	0.017	0.415
67	Cholecystectomy	70	Brown	Much	Acid	Positive	Negative	0.148	0.019	0.284
68	Hemorrhoids	78	Brown	Little	Acid	Positive	Positive	0.137	0.020	0.387
69	Hemorrhoids	63	Green	Much	Acid	Negative	Positive	0.134	0.036	0.366
70	Hemorrhoids	37	Green	Little	Acid	Positive	Positive	0.120	0.036	0.415
71	Umbilical hernia	70	Gray	Moderate	Acid	Negative	Positive	0.120	0.036	0.437
72	Colostomy	70	Yellow	Much	Acid	Negative	Negative	0.216	0.017	0.383
73	Gall-bladder	70	Green	Little	Acid	Negative	Positive	0.109	0.031	0.412
74	Bunion	43	Gray	Moderate	Acid	Negative	Negative	0.129	0.027	0.380
75	Hernia	31	Green	Little	Neutral	Negative	Negative	0.193	0.036	0.621
76	Hemorrhoids	41	Gray	Little	Alkaline	Negative	Negative	0.182	0.032	0.366
77	Hernia	95	Green	Much	Acid	Negative	Positive	0.117	0.013	0.398
78	Appendicitis	80	Brown	Moderate	Acid	Positive	Positive	0.098	0.012	0.348
79	Osteomyelitis	80	Gray	Much	Acid	Negative	Positive	0.174	0.029	0.330
80	Appendicitis	30	Green	Much	Acid	Positive	Negative	0.140	....	0.479
81	Hernia	31	Gray	Little	Acid	Negative	Negative	0.160	0.030	0.465
Average								0.147	0.022	0.378

Ratio of ammonia to total nitrogen, 1 to 6.6.

Total of nitrogen to chlorine, 1 to 2.6.

This result points to a conclusion that Congo paper is hardly sensitive enough to rely on even for a qualitative test, and to use instead, according to Leo, a solution of Congo red, which is much more delicate than the paper. He shows that while Congo paper gave a positive reaction when 0.01 per cent. HCl was present, a solution of Congo red gave a positive reaction with but 0.0009 per cent. HCl.

The presence of bile in 56 of the specimens and its absence in 25 was rather interesting. Bile in the gastric secretion occurs as a regurgitation into the stomach—frequently seen in the vomitus whenever the vomiting may be very intense or frequently repeated. The presence of bile, ever so faint, signifies an antiperistalsis of the duodenum. Larger amounts of bile point to a deficient stomach motility, an atony, or an ectasia. Schüler even says that large amounts of bile aid in making a differential diagnosis between an atonic ectasia and an ectasia due to a pyloric stenosis, being much larger in amount in the former.

The passage of bile into the stomach during digestion seems, according to several observers, to have no disturbing action on gastric digestion. The acid contents of the stomach, containing an abundance of proteins, gives with the bile a precipitate of proteins and bile acids. The precipitate formed easily redissolves in an excess of bile, and also in the NaCl formed by the neutralization of the HCl of the gastric juice. This may take place even in a faintly acid reaction.

The chemical reaction of bile is feebly alkaline, and when in the stomach unquestionably neutralizes the HCl, and this perhaps accounted for the small number of Congo positive reactions. Of the 27 positive Congo reactions, 16 showed the presence of bile; of the 53 negative Congo reactions 40 showed the presence of bile.

From this it can be assumed that, while the bile has but little influence on the acid reaction to litmus, it does appear to have some effect on the Congo reaction. There were but 9 cases in which the reaction was alkaline, and in 6 of these bile was present. In these 6 cases the chlorine percentage was comparatively high, while in the other 3, in which bile was absent, this percentage was low.

The percentage of total nitrogen varied from 0.014 to 0.362, the average being 0.147. In recent years more attention has been given to the nitrogen content of the gastric secretion, particularly by Salmon for the purpose of diagnosing carcinoma of the stomach. He maintained that if in 100 c.c. of normal salt solution used to rinse out the empty stomach, he found more than 25 mg. of total nitrogen, it indicated the presence of a carcinoma. In none of the patients from whom the specimens were obtained was carcinoma diagnosed, thereby preventing confirmation of his opinion.

Ammonia in the stomach secretion is regarded by some as a pathological constituent, by others (Rosenheim and Strauss) as normal. In each of the 81 specimens the ammonia content was a fairly constant one, as will be seen from the table—an average of 0.022 per cent.

Chlorine, a normal component of the gastric juice, is a most important element for the formation of the HCl. How this acid is formed we are not at all certain. According to the older observers, the amount of chlorine present in gastric juice is more than would suffice to form chlorides with all the bases present, and the excess, if regarded as existing in the form of HCl, corresponds exactly to the amount of free acid present. At some subsequent time I shall publish results on this question.

Looking at the chlorine figures, it can be seen that these vary considerably. Realizing that chlorine enters materially into the quantity of HCl formed, we find that a positive Congo reaction was obtained when there was 0.27 per cent. or upward of chlorine.

Although 60 of the cases showed the presence of more than 0.30 per cent. chlorine, the Congo reaction was positive in 24 and negative

in 36. Of the positive ones, bile was present in 14 and absent in 10. Of the 36 negative cases, bile was present in 29 and absent in 7. From this we may be permitted to conclude that the bile present in some way acts on the chlorine and hence gives a negative Congo reaction. This appears to indicate that bile in the stomach—how frequently it is present we can not say, because we assume it is only present as a result of vomiting or in pathological conditions—influences the acidity, and may be used therapeutically in cases of hyperacidity with at least similar or perhaps better results than attend the use of alkalies. At present I am engaged in a study of this question, and in a subsequent communication will give my results.

In making studies on the total nitrogen, ammonia, and chlorine contents of the gastric juice, one must not lose sight of the saliva factor. To allow for this, I examined these elements in ten normal salivas.

TABLE II.—SALIVA.

No.	Total nitrogen.	Ammonia.	Chlorine.
1	0.0616 per cent.	0.0085 per cent.	0.0568 per cent.
2	0.0504 per cent.	0.0085 per cent.	0.0852 per cent.
3	0.0658 per cent.	0.0238 per cent.	0.0816 per cent.
4	0.0546 per cent.	0.0187 per cent.	0.0461 per cent.
5	0.0826 per cent.	0.0255 per cent.	0.0994 per cent.
6	0.0546 per cent.	0.0120 per cent.	0.0460 per cent.
7	0.0434 per cent.	0.0050 per cent.	0.0710 per cent.
8	0.0364 per cent.	0.0170 per cent.	0.1171 per cent.
9	0.0546 per cent.	0.0170 per cent.	0.0532 per cent.
10	0.0644 per cent.	0.0153 per cent.	0.0710 per cent.
Average	0.0568 per cent.	0.0151 per cent.	0.0727 per cent.

Ratio of ammonia to total nitrogen, 1 to 3.76. Total of nitrogen to chlorine, 1 to 2.28.

From these ten cases an average was obtained for comparison with the same constituents of the gastric secretion, and it will be noticed that the total nitrogen in the latter is almost three times that of the saliva, the ammonia twice, the chlorine more than five times.

To Dr. S. Bookman, thanks are due for many suggestions in the course of this study.

**LOCAL ASPHYXIA OF THE EXTREMITIES (RAYNAUD'S DISEASE)  
WITH THE HITHERTO UNDESCRIBED COMPLICATION OF  
INTERMITTENT ACHYLIA GASTRICA.**

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LOCAL asphyxia and symmetrical gangrene are not two different diseases, but two degrees of one and the same malady. The latter condition is often absent. While the word "asphyxia" expresses a definite pathological state, the term "local" may be misleading, since, according to Raynaud, search for the origin should not be confined to the affected parts. The following case was first seen at the Beth-Israel Dispensary, January 12, 1909.

Celia R., aged twenty-three years, single, a dressmaker, born in Russia, has lived two and one-half years in America.

**Family History.** Father and a paternal uncle have hemorrhoids; mother is "very nervous;" one brother has chronic indigestion; sister is subject to attacks of long-lasting singultus. There is no history of a disease like the patient's.

**Personal History.** Hygienic surroundings are poor; the diet is mixed; no alcoholic beverages are used; tea and coffee in moderation. Although she can eat everything, the patient does not enjoy her food.

**Previous Diseases.** Has had the ordinary diseases of childhood. Five years ago in Russia had malaria. Syphilis is denied.

**Menstrual History.** Menstruation began at the age of fourteen years; interval twenty-eight days; duration four to seven days; flow profuse; pain present for two days. For the last three years there has been some irregularity in the interval, which is now only two or three weeks.

**Present Illness.** Dates back to her malaria, five years ago. At first the fever was quotidian in type, the attacks lasting several hours. After several weeks the hyperpyrexia and sweating began to occur every other day. Then for three months large doses of quinine were given. The patient remained very weak and was under medical care for three months more. Soon after she recovered from her post-malarial weakness she noticed that one finger of the right hand (which one she cannot remember) became white and "dead." Motion was normal, but sensation was lost. The whiteness extended to all the phalanges of both hands, and remained unchanged for a year's time, when the skin began to assume a bluish aspect, while loss of sensation and coldness became quite marked. Later the feet became similarly affected. The condition, improving somewhat in summer, is worse on cold winter days. The patient notes that even

on hot days she does not sweat like other people, and is not compelled to change her underwear more frequently in summer than in winter, although it very seldom happens that a few drops of cold perspiration appear on the forehead.

**Physical Examination.** The skin, especially that of the face, is dry, very tense, and lacking in elasticity. For the last reason drawing the inferior eyelid from the eyeball is possible only with difficulty, and the upper lid droops somewhat. It is almost impossible to raise the skin of the extremities and face in folds. Both hands have a bluish appearance, and to the touch they are dry and icy cold. The feet, especially the toes, feel the same, but have not the bluish appearance of the hands. The fingers of both hands are spread and held in slight flexion. Complete extension is impossible.

With the exception of a few small areas where sensation is diminished, the skin, together with the mucous membrane of the anterior part of the tongue, is entirely insensitive to pinpricks. The temperature is quite lost in the affected parts of the hands and feet and is much diminished over the greater part of the remainder of the skin. The tactile sense is somewhat perverted. The muscular sense and the stereognostic sense are normal. The knee-jerks and the Achilles-jerks are slightly exaggerated. There is no ankle clonus.

The circulatory apparatus is normal. The pulse is palpable in the posterior tibial, and in the dorsal artery of the foot, as well as in the radial. No thickening of the arterial wall can be detected. The blood pressure is 130 mm. Hg. Neither the liver nor the spleen is palpable.

The pupils are equally dilated. There is slight blepharitis. The papillæ are of normal color; the arteries contracted, their lumen being about one-half that of the veins. There is slight hypermetropia (R., 0.5; L., 0.25). Otherwise the eyes are normal.

**The Blood.** Hemoglobin, 80 per cent.; the red cells, 6,030,000; the color index, 0.66; the leukocytes, 7400. Differential count: Polymorphonuclears, 280 (70 per cent.); large mononuclears, 16 (4 per cent.); small mononuclears, 83 (20.75 per cent.); transitionals, 8 (2 per cent.); eosinophiles, 10 (2.5 per cent.); basophiles, 0 (0 per cent.); unclassified, 3 (0.75 per cent.). The red cells vary slightly in size and shape. No malarial plasmodia and no free pigment were found.

The urine was examined six times. The twenty-four-hour amount varied from 950 to 1450 c.c. The acidity (using one drop of phenolphthalein as an indicator and titrating with decinormal sodium hydrate solution) varied from 30 to 60. Neither albumin nor sugar was ever found. Indican was present to slight excess. The centrifuged sediment contained an excess of urates. Casts were never found.

A radiogram of the hands show some slight absorption of bone in the phalanges (Figs. 1 and 2).

*The Stomach Contents.* January 14: One hour after an Ewald-Boas test breakfast, 8 c.c. of very thick and nearly dry material, with a very little fluid and some exceedingly tenacious mucus, was expressed. It took some time to clear the tube of the particles of roll, which appeared absolutely unchanged. It was evident that no chymification was going on. Free HCl, negative to Congo red and to philoro-



FIG. 1.—Radiogram of the left hand, showing slight absorption of bone in the metacarpals.

glucin-vanallin. Maltose (with Fehling's solution), positive. Lactic acid, negative. Total acidity, not determined. On the same morning the acidity of the urine was 60. The hands, especially the fingers, were blue, the feet a little less so. (It was a very cold day.)

January 16. Ewald-Boas breakfast eaten at 9 A.M., expressed at 10. Amount about 20 c.c., of the same gross appearance as the last.

Mucus, present. Free HCl, negative. Total acidity, 8. Rennet, pepsin, and lactic acid, negative. Acidity of the urine, 58. The fingers and toes very blue.

January 18. One hour after a similar breakfast, 30 c.c. was expressed. This was more fluid and there was no mucus. The particles of roll were much changed, as if chymification were pro-



FIG. 2.—Radiogram of the right hand, showing absorption of bone in the metacarpals. Similar to that seen in the left hand.

ceeding. Free HCl, 8. Total acidity, 28. Acidity of the urine, 48. The fingers and toes had no suggestion of blueness.

On six later occasions the gastric contents were examined after a test breakfast. Twice free HCl and pepsin were absent, mucus was present, and the total acidity was less than 12. These findings corresponded to those cold days when the symmetrical asphyxia and the cyanotic appearance of the extremities were most marked. On two



of these days the eyegrounds were examined, with the results already noted. On the days when free HCl was present (ranging between 4 and 8) and the total acidity reached 20 or 30 (once as high as 40) the fingers and toes looked red.

To recapitulate, we see: (1) That the patient belongs to a neurotic family. (2) That as far as the presence of hemorrhoids points to an angioneurotic condition there is this predisposition also; but that the patient herself is not neurasthenic nor hysterical. (3) That she was in perfect health until the age of eighteen, when, soon after an illness with an obstinate form of malaria, she noticed the development of her present malady. (4) That though the condition of all four extremities is better in the summer, yet even then her skin does not functionate so actively as the skin of other people. (5) That the pain sense is lost not only in the affected parts, but nearly all over the skin and on the anterior part of the tongue, with diminution of the senses of temperature and touch. (6) That while the heart and palpable vessels are normal, the small arteries of the fundus show a marked contraction when the asphyxia of the extremities is most pronounced. (7) That there is a slight secondary anemia. (8) But the most striking feature is the fact that, without dyspeptic symptoms, there is a lack of free HCl and the presence of mucus in the stomach contents on those days when the fingers and toes show the most characteristic picture of local asphyxia; while on the days when the extremities are red no mucus is present and the quantitative examination shows merely hypoacidity.

In the literature we find malaria mentioned as a relatively frequent cause of local asphyxia, which may develop to a slight degree in the course of intermittent fever. Raynaud<sup>1</sup> was aware of the intermittent character of the disturbance, and also of the fact that, after the fever has subsided the convalescent may suffer from attacks of local asphyxia. He gave quinine in such cases. Of this his Cases V and VIII are good illustrations. (Case V.—Woman attacked by tertian fever in March. Local asphyxia and cyanosis noted in April. Case VIII.—Woman ill for three months with tertian fever. A few months later local asphyxia intervened.) Petit and Verneuil<sup>2</sup> report cases in which fever preceded the local asphyxia for years, and insist on the importance of the former as a cause. Brehier (quoted by Monro<sup>3</sup>) goes even so far as to suggest that local asphyxia is but a latent form, "*une forme larvée*," of malaria. Again, Petit and Verneuil point out that the malarial poison is not sufficient, but that there must be other etiological factors, and that exposure to cold is probably one of these. In our case no history of the latter cause could be elicited.

<sup>1</sup> Local Asphyxia and Symmetrical Gangrene of the Extremities. Translated by Thomas Barlow; Selected Monographs; New Researches on the Nature and Treatment of Local Asphyxia of the Extremities. Translated by Thomas Barlow.

<sup>2</sup> *Revue de chirurgie*, 1883.

<sup>3</sup> Raynaud's disease.

According to Raynaud himself, the site of the lesion is probably in the cord, and so the symmetry of the affection is explained, as well as the good results following the application of a descending current to the spine. Mourson (quoted by Monro) thought the vascular spasm to be due to irritation of the vessels of the cord by melanemic deposits. This pathological condition might be present in my patient, although free pigment was not demonstrated in the blood. The peculiar skin, with the history of anidrosis even in the intervals between the attacks of local asphyxia, would speak for some form of scleroderma, a complication not so rare in Raynaud's disease. Stürmdorf<sup>4</sup> describes an analogous picture of the skin, especially that of the face, "*la masque sclérodermique*" of the French. The near approach to anesthesia of the skin, with the much diminished acuity of the temperature sense and tactile sense, suggests syringomyelia. One of Braman's<sup>5</sup> cases was very similar to ours. Although anesthesia is very frequent in hysteria and, according to Osler,<sup>6</sup> the concurrence of Raynaud's disease and hysteria is common, the patient did not exhibit any of the ordinary stigmas of hysteria, and the distribution of the anesthetic areas was always the same.

The contraction of the papillary arteries would give more support to the theory that local asphyxia is a neurosis in which the local symptoms are due to spasm of the arterioles. Fox<sup>7</sup> reports a case of sudden paroxysmal impairment of vision, with such changes in the arteries of the fundus. My patient had no disturbance of vision. The eyegrounds were examined simply because Raynaud called attention to the changes therein. According to his views this condition is not associated with spasm of the arteries of greater size. Calmette (quoted by Monro) showed that patients, who have recently suffered, or are still suffering, from malarial cachexia exhibit paroxysmal narrowing of the papillary vessels.

Some explanation must be given of the radiogram of the patient's hands, taken by Dr. Isaacs, to whom I take this opportunity to express my hearty thanks. This shows some very slight absorption of bone. Carl Beck<sup>8</sup> is of the opinion that the tissue changes in Raynaud's disease are not confined to the soft parts, but affect the bones as well. He reports two cases with radiograms to prove this assumption.

The examinations of the urine showed simply an excess of uric acid crystals and a varying degree of hyperacidity. Haig (quoted by Monro) thinks many symptoms of Raynaud's disease resemble those

<sup>4</sup> Symmetrical Gangrene, Medical Record, 1891

<sup>5</sup> Fälle symmetrischer Gangrän, Verh. d. Deutsch. Gesellsch. f. Chirurg., 1889, xxix, 37.

<sup>6</sup> The Cerebral Complications of Raynaud's Disease, AMER. JOUR. MED. SCI., November, 1901.

<sup>7</sup> Two Cases of Raynaud's Disease with Ocular Symptoms; One Case Complicated by Scleroderma, Jour. Cutaneous Dis., August, 1907.

<sup>8</sup> Some New Points in Regard to Raynaud's Disease, AMER. JOUR. MED. SCI., November, 1901.

of "uric acidemia," and in one severe case he was able to demonstrate a great excess of uric acid in both the blood and the urine. He believes that uric acid causes the contraction of the arterioles.

We come now to a consideration of the gastric analyses. After the second examination we thought that the anacidity was of nervous origin, as the patient was not suffering from any disease which might lead to achylia gastrica, such as pernicious anemia, nephritis, or tuberculosis. Slight secondary anemia was indeed diagnosed, but such a condition would not be sufficient to cause any marked chemical changes in the gastric secretion. The fact that the patient did not exhibit any subjective symptoms of gastric disturbance would not exclude achylia gastrica. Knud Faber and Lange<sup>9</sup> published not long ago several cases (Cases VII to XI of their series) which ran along without any symptoms and without demonstrable cause.

The presence of mucus speaks against achylia gastrica, if we accept Einhorn's<sup>10</sup> use of the term, since he requires absence of mucus to establish such a diagnosis. A gastric catarrh, on the other hand, with anacidity would not exist for any time without symptoms. Moreover, the patient is much younger than the average sufferer from this disease, and the analyses showed a varying condition of the gastric secretion. In catarrh of the stomach the findings are usually constant. Some other explanation for this variation must be sought. In spite of Hayem's disbelief in nervous achylia gastrica, we must agree with Einhorn that such a form probably does exist, especially since his well-known illustrations give strong support to his opinion. I would classify my case as one of paroxysmal achylia gastrica and paroxysmal mucorrhœa, and would submit that the same etiological factor produces both affections, together with the attacks of local asphyxia in the extremities and the changes in the eyegrounds; and that if the last, as is unquestionably the case, is due to spasm of the arterioles, so may be all the preceding. It is not unlikely that all the above symptoms should occur together, or that the gastric symptoms should be caused by arterial spasm and vary with the intensity of the spasm.

It is, indeed, possible that there are two types of achylia gastrica: The first, of nervous origin, would take the form of a paralysis of the secretory fibers to all of the gland cells; the second, of vascular origin, would cause rather a temporary asphyxia of the same cells, with a resulting alteration in the secretion. Pawlow<sup>11</sup> points to the peculiar changes in the gastric juice following section of the vagus as evidence of the role played by the sympathetic in exciting the changes. Sympathetic and vagus seem to extend mutual aid in the performance

<sup>9</sup> C. Lange, Die Pathogenese u. Aetiologie der chronischen Achylia Gastrica, Ztschr. f. klin. Med., 1908, 66.

<sup>10</sup> A Further Report on Achylia Gastrica, Medical Record, 1905.

<sup>11</sup> The Work of the Digestive Glands. Translated by W. H. Thompson, 1902.

of this function. Now, as is well known, the sympathetic is much richer in vasoconstrictor fibers than the vagus, and it is not unlikely that it influences gastric secretion chiefly through its action on the arterioles of the gastric mucosa. Stimulation of the sympathetic was held by Raynaud to be responsible for the spasm of the retinal arteries, as well as of the arterioles of the extremities, on which, in turn, depends the local asphyxia. The experiments of Adamiuk (quoted by Raynaud) are of interest in this connection, for he states that if in a curarized animal the sympathetic ganglion at the level of the seventh and eighth cervical vertebræ be stimulated, an ophthalmic examination will reveal the same distribution of blood as in glaucoma, that is, the veins are greatly distended and the arteries contracted.

In my case, although contraction of the papillary arteries and achylia gastrica were found together on two occasions, no coincidence of the opposite conditions, namely, normal eyegrounds and normal gastric secretion was demonstrated. However, the achylia and the cyanosis did appear and disappear together. It is easily conceivable that a spinal irritation might result in contraction of the vessels of four different regions, *e. g.*, hands, feet, retina, and stomach. The double innervation of one of these regions corresponds to that of the salivary glands. By stimulating the cerebral fibers running to the submaxillary gland in the chorda tympani, an abundant secretion of thin liquid is produced; if the sympathetic be stimulated, only a few drops of viscid fluid are secreted. The sympathetic fibers have been shown to end around the vessels of the gland.

Furthermore, we know from the experiments of Claude Bernard (quoted by Abderhalden<sup>12</sup>) that if the lingual nerve which carries the cerebral fibers to the submaxillary gland be cut and the peripheral end stimulated, the bloodvessels in the gland become distended and the blood in the veins assumes a bright red color similar to that of the arterial blood. At the same time there is an increased secretion of saliva. On the other hand, by stimulating the fibers of the sympathetic the bloodvessels are contracted, the blood streams more slowly, and the flow from the veins is small in amount and of a dark red color. It is fair to say that in the latter condition the activity of the secretion is diminished because of the stasis in the veins or a local asphyxia of the glandular tissue. It is true that Heidenhain showed that the innervation of the bloodvessels is not the sole function of the above-mentioned nerve, yet it is unquestionably an important one. In like manner the secretion of gastric juice depends not wholly on vagus action, but to some extent also on that of the sympathetic, although the action of the latter alone results in an abnormal secretion containing but little pepsin. In our case the gastric contents showed none of the ferment and very little liquid.

<sup>12</sup> Text-book of Physiological Chemistry. Translated by Wm. T. Hall.

A few further references may be of interest. Valentine Calonne,<sup>13</sup> in his exhaustive thesis on the subject of Raynaud's disease and its complications, says that disturbances of the gastro-intestinal tract are very rare. Abercrombie<sup>14</sup> narrates the history of a boy, aged three years, who, before the onset of asphyxia was very "yellow," and who when his hands were cold cried on account of the pain in his stomach. When his hands became warm again, the pain in the belly disappeared. Paroxysmal hemoglobinuria was also noted in this case. One of Fox's patients suffered from nausea in the morning, and often vomited after eating. A second patient of his with gastro-intestinal disturbance complicating Raynaud's disease vomited frequently after eating and had frequent attacks of diarrhœa. It is possible that the diarrhœa was due to the achylia, a common cause of this condition. The attacks might indicate a spasm of the arterioles in the gastric glands, and an analysis of the stomach contents, had it been made, might have shown the same condition of intermittent achylia as in my case.

## CLINICAL OBSERVATIONS IN HEART-BLOCK.

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BRADYCARDIA, dyspnœa, and loss of consciousness or convulsions were first described as a symptom group by Morgagni, about 1750, followed by Stokes, in 1846, Adams, in 1872, and was given the name of Stokes-Adams disease by Huchard, in 1893. The discovery of the atrioventricular bundle by Kent in cold-blooded, and by His in warm-blooded, animals, and later in man, stimulated study of the functional relationship of auricle and ventricle, resulting, through the experimental and clinical work of Hering and Erlanger, in the recognition of the association of conditions of heart-block and the Stokes-Adams syndrome. Extended clinical knowledge has shown the error of the earlier opinion that these conditions are identical, for it is now recognized that either may exist without the other. There may be heart-block without the Stokes-Adams symptoms and Stokes-Adams symptoms without heart-block. The following cases are put on record to emphasize this well, though somewhat newly, recognized fact, and to contribute to the literature a few clinical observations of a sort that must be

<sup>13</sup> Associations pathologiques dans la maladie de Raynaud, Paris, Thèse, 1904.

<sup>14</sup> Some Points in Connection with Raynaud's Disease, Arch. of Pediatrics, 1886, 567, 573.

much more numerous and extensive before any final classification of the various types of the complex condition can be made. Two of the cases illustrate heart-block with, and one heart-block without, the Stokes-Adams syndrome.

*CASE I.—Heart-block with Stokes-Adams Syndrome.* The patient, a housewife, aged sixty years, has been twice married and has four living children, one of whom, a daughter, has a congenital heart lesion. She has always eaten well, used wine and whiskey daily, coffee in moderation, and taken no exercise. She has been obese for years. There has never been a serious illness, but she has suffered several nervous shocks and had much responsibility.

The present illness began in 1906, with shortness of breath on exertion, while the patient was living at an altitude of 7000 feet. There was no other trouble until June, 1908, when, after dancing at night and running for a train the next day, there was unusual exhaustion. The day following, on the train, there was a sudden fainting attack, and the day after, the patient fell in the street in syncope, revival being immediate. At this time a physician found the pulse rate 20. Observation has since been continuous. During June, 1908, there were one or two syncopal attacks a day. Confinement in bed was enforced, and by July these subsided, the pulse rate rose to 45, and the patient went about without trouble, until September, when the pulse was 25 and there were renewed faints. On November 8, 1908, the pulse became 20, then 15, and later 12. With this were serious faints and epileptiform convulsions, numbering, at most, twenty a day. Tincture of digitalis in five-drop doses was given, and coincidently the pulse rate rose to 25 and there was steady improvement. Later the pulse rose to 35, when the convulsions and syncopal attacks ceased. The patient crossed the continent, and en route, at an altitude of 7000 feet, the pulse was 70. Upon reaching New York it was 65. On December 7, 1908, the pulse tracings reproduced as Fig. 1 were made.

*Physical Examination.* December 11, 1908. The patient is stout and of good color. The heart is not enlarged to percussion; it shows a slight harsh systolic murmur at the apex and at the base; the latter is heard over the aorta. The pulse rate is 48 to 60, changing suddenly from one to the other. The arteries are full and slightly thickened. The arterial pressure is systolic, 170 mm. Hg.; the diastolic, 80 mm. Hg. The liver edge is just palpable. There is no œdema. The knee-jerks are active.

*Clinical Course.* During the next week the pulse rate varied between 38 and 56, and there were no symptoms. On December 24, 1908, the rate fell to 30 and there was discomfort, but no syncope. No intermediate heart sounds could be heard. Tincture of digitalis, 5 minims three times daily, and strychnine sulphate,  $\frac{1}{16}$  grain every third hour, were given. The tracings shown in Fig. 2 were taken on this date.

On December 25 there was a questionable syncope in the night, the pulse rate being 28 to 32. December 28 and 30 were spent in bed, there being vertigo when sitting up, but no faints. Tincture of digitalis was stopped. The tracings shown in Fig. 3 were made.

On January 4, 1909, the pulse rate was 26 to 32. There was dyspnoea, the apical systolic murmur was more pronounced, the liver moderately enlarged, and slight oedema of the legs was present. On January 13 the patient was more comfortable. The oedema had disappeared. The tracings shown in Fig. 4 were made.

During the next two weeks tincture of digitalis, 10 minims three times a day, was given and the pulse rate rose from 25, on January 15, to 34 on the 27th, and 40 on the 29th, when the drug was stopped. Atropine given in quantity sufficient to produce dryness of the throat and flushing caused no change in the pulse. On January 27 there was a slight epileptiform convulsion, during which the pulse was 34. The tracings shown in Fig. 5 were made about one hour later. On January 29, the tracings, shown in Fig. 6, were made.

On February 6 there was complete syncope while automobiling. No change was observed in the pulse, the rate being 36 to 38. Faint intermediate sounds were noted. From February 16 to 27, tincture of digitalis, 10 minims three times a day, was given without influence upon the pulse rate. On March 4 the patient had been comfortable, except for restlessness and slight dyspnoea at night. No faints have occurred until this date, when there was a convulsion. The pulse rate has been 26 to 32 of late. On March 7 there was a severe convulsion with marked cyanosis at 10 A.M. The pulse, observed by the husband, was said to have been 110 during the attack. Ten minutes later it was 30. On March 9, nocturnal, paroxysmal pain with slight dyspnoea, suggesting anginal attacks, was a complaint. There was evident slow cardiac enfeeblement. The heart sounds were faint, the rate 31. The liver was enlarged and slightly tender. There was no oedema. On March 11 there was weakness and vertigo, the usual prodromal symptoms of an attack. Nitroglycerin,  $\frac{1}{100}$  grain, taken immediately caused pain and throbbing in the head, but apparently aborted the paroxysm. The pulse rate was 39. On March 13 nitroglycerin taken several times for precordial distress gave in each instance complete relief, and the patient felt better and looked better than for three months. The pulse rate varied between 26 and 62. On walking, the rate rose from 38 to 45, again slowing after a short time. On March 20 the pulse rate varied between 30 and 72, the husband once volunteering the observation that it suddenly dropped from 72 to half this. The patient walked about without distress, and nitroglycerin always relieved unpleasant symptoms. The tracings shown in Fig. 7 were made. After exertion and after nitroglycerin these showed no change.

April 20. The patient has been going along without incident during the past month, excepting a slight faint on April 19. The pulse rate has been constantly between 27 and 32. Today there was a convulsion. At the start the pulse was 28, as previously; then very slow; then full and about 80; then 35, and the attack ceased. Later the pulse was again 28. On April 21 there was vertigo in the night.

April 28. The pulse rate has been between 25 and 28 and the patient has been comfortable until the last three days, when there has been epigastric distention and distress, insomnia, dyspnoea, moderate orthopnoea, but no faints. There are present signs of slight cardiac insufficiency, a little cyanosis, a more marked systolic murmur at the apex, the pulse of a lower tension than before, the liver edge four inches below the costal border, and slight oedema of the ankles. Tincture of digitalis, 10 minims three times a day, was ordered, and the patient left for the country, where she is continuing comfortably and without event.

October 25, 1909. The pulse rate during the summer has been constantly between 28 and 34, with no change in the general symptoms and with but one convulsion and two syncopal attacks. On October 1, 1909, the pulse rate suddenly became 80 and has since varied between 60 and 90, with disappearance of oedema, dyspnoea, and other evidence of cardiac difficulty. The patient can go up four flights of stairs without trouble, is walking unrestrictedly, and feels perfectly well.

*Analysis of Tracings.* These were made with a modified MacKenzie polygraph. This instrument in its original form proved so inefficient and time-consuming as to compel its abandonment had not certain changes been worked out. These are: (1) The addition of a screw adjustment to the radial receiving tambour, making possible delicate changes in pressure on the artery; (2) the introduction of outlet valves in the air transmission for the ready adjustment of air pressure. This was done by perforation of the receiving jugular cup, the hole being covered by the finger during use; and placing a T-tube with clip in the arterial transmission; and (3) the use of a very dilute solution of methylene blue, reducing viscosity and consequent friction of writing points to a minimum. At best, however, the instrument is far from satisfactory and scarcely to be recommended for routine use.

The tracings shown in Fig. 1, recorded December 7, 1908, show simultaneous radial and jugular tracings that at first glance might be thought normal. The auricular rate is 60, the ventricular also 60. There is a complete *a-v* association. Measurement of the *a-c* interval brings to light the first graphic suggestion of trouble in the His bundle. Here the conduction time is increased from the normal one-fifth of a second or less, to one-fourth or one-third second. This observation, together with the history of the case, confirmed



the diagnosis of Stokes-Adams syndrome before the more definite later evidence was obtained.

Fig. 2, recorded December 24, 1908, shows an auricular rate of 90, a ventricular rate of 30. The jugular tracing shows waves of the auricular type occurring at approximately regular intervals, every third wave being followed, with slightly delayed conduction, by a ventricular contraction—the picture being clearly that of a partial *a-v* dissociation with a rhythm of 3 to 1. Events within the

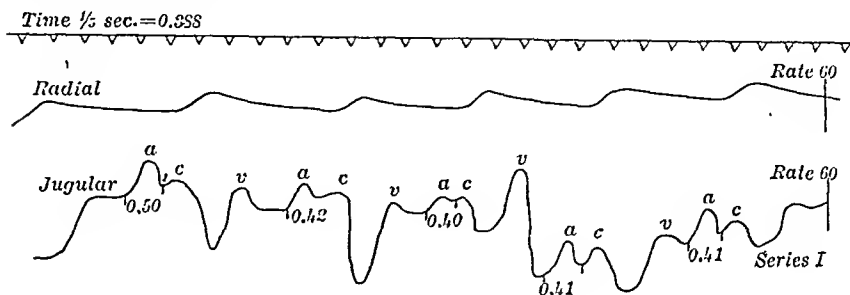


FIG. 1

ventricle may be followed by study of these groups of *a* waves. It is seen that the *a'* wave, that immediately succeeding ventricular systole, is followed by a marked negative wave due to the negative pressure in the empty and relaxing ventricle. The negative phase of the *a''* wave is less pronounced, thus illustrating the accumulation of blood in the inactive ventricle.

Fig. 3 shows an auricular rate of 90, a ventricular of 23, a complete *a-v* dissociation. This tracing is of interest in showing the interrelation of the *a* and *c* curves when there is independence of

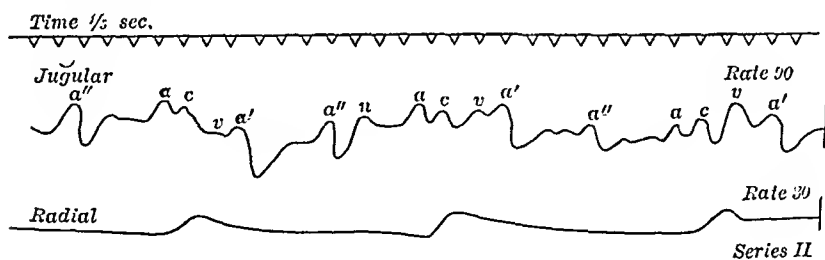


FIG. 2

auricle and ventricle. The curve (1) of broad summit can only be due to the close following of the *a* wave upon the *c*. Measurement of the auricular intervals shows this to be the case. Following the next *c* wave (2) is the *a* wave, high because of the resistance of the still contracting ventricle, and followed by a marked negative wave at the conclusion of ventricular systole and synchronous, therefore, with the dicrotic notch on the carotid tracing. The third *c* wave is very small and hardly differentiated from the *a* wave

immediately preceding. The auricular contraction has started a current of blood through the auriculoventricular orifice. This is met by a counter impulse arising from the slightly later ventricular contraction, and the resultant of these two forces is the lessened

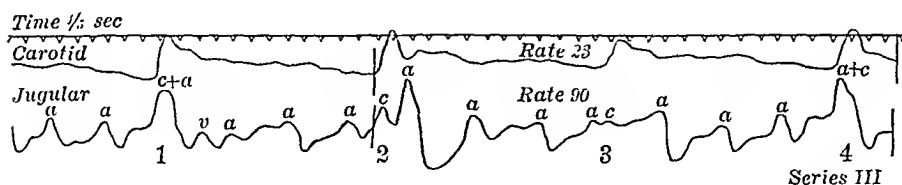


FIG. 3

*c* wave. The auricle, unable to discharge its contents fully, remains filled until the next *a* wave, when there is a prominent negative phase marking the egress into the relaxed ventricle.

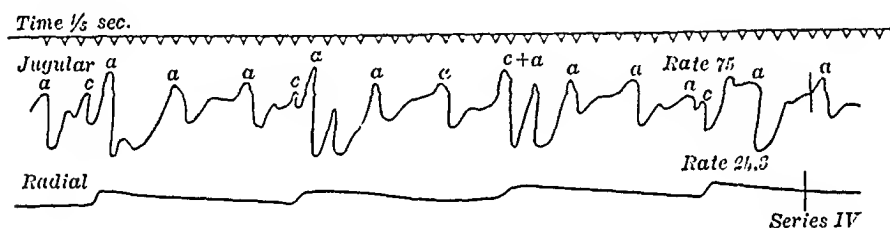


FIG. 4

Fig. 4, recorded January 13, 1909, shows an auricular rate of 75, a ventricular of 24.3, just missing a 3 to 1 rhythm, nevertheless a completely dissociated auricle and ventricle.

Fig. 5, recorded January 27, 1909, shows a condition similar to that of Fig. 4, the rate being more rapid—auricular, 90; ventricular, 29.

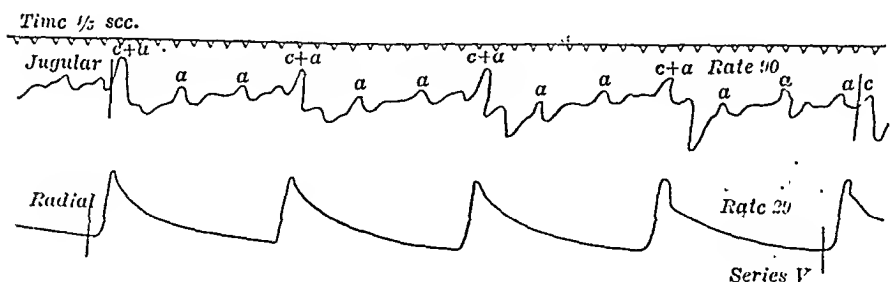


FIG. 5

Fig. 6, recorded January 29, 1909, shows an auricular rate of 93, a ventricular of 34, continued *a-v* dissociation. The series is distinguished by unusually prominent *n* waves. The *n* wave was first described by Erlanger and three possible factors in its causation

mentioned. These are: (1) A reflux wave from the auricle, due to the accumulation of blood within its chamber previous to auricular systole. This alone is an inadequate explanation, as such a wave could have no negative phase. (2) The occurrence of a presystolic wave in the great waves of the neck. (3) The reciprocal variation in pressure upon either side of the auriculo-ventricular valves during diastole caused by intermittent relaxation

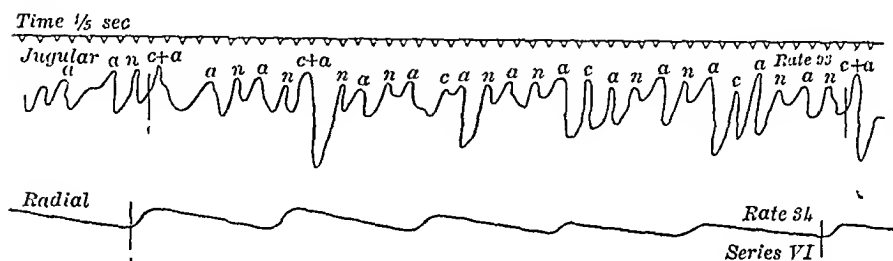


FIG. 6

of the ventricle. This gives rise to both positive and negative waves in the auricle and contributory great veins.<sup>1</sup>

Fig. 7, recorded March 20, 1909, shows an auricular rate, 78.3; ventricular, 39.15, an exact 2 to 1 rhythm. Such return to a partial *a-v* association after a prolonged period of completely dissociated auricle and ventricle is an argument against Nogoyo's statement<sup>2</sup> that complete *a-v* dissociation is proof of complete destruction of a segment of the His bundle, and therefore calls in question the accuracy

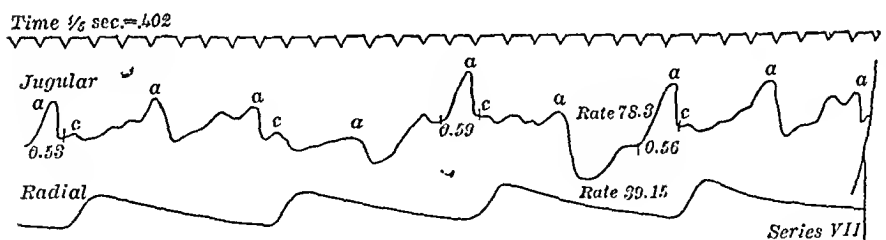


FIG. 7

of the division of the Stokes-Adams symptom complex into (1) the conduction type with complete dissociation and as a pathological basis, the complete division of the atrioventricular node, and (2) the muscle type, with only partial dissociation and the lesion a degenerative change in the heart muscle itself.

The tracings reproduced as Fig. 8 show complete *a-v* association with greatly delayed conduction. Such resumption of complete

<sup>1</sup> Von Frey and Krehl, *Archiv f. Phys.*, 1890, xxxviii.

<sup>2</sup> Pathologisch-anatomische Beiträge zum Adams-Stokesschen Symptomkomplex, *Ztschr. f. klin. Med.*, 1909, lxxvii, 495.

*a-v* association after nine months of partial or complete *a-v* dissociation with disappearance of all symptoms is of special interest in considering the prognosis of heart-block.

Renewal of *a-v* association after a complete dissociation demonstrates, in so far as mere clinical observation can, that complete heart-block may exist without permanent solution of continuity of the atrioventricular bundle. That this effect was in this instance due to improved nutrition of the bundle through vasodilatation resulting from the action of nitroglycerin seems probable; and points to a sclerosis of the artery supplying this area as the most likely pathological basis of the case. This view is strengthened by benefit derived from digitalis whenever the heart muscle showed signs of failure. The improved nutrition of the bundle more than counterbalanced the usual evil effects of digitalis when there is impaired conductivity.

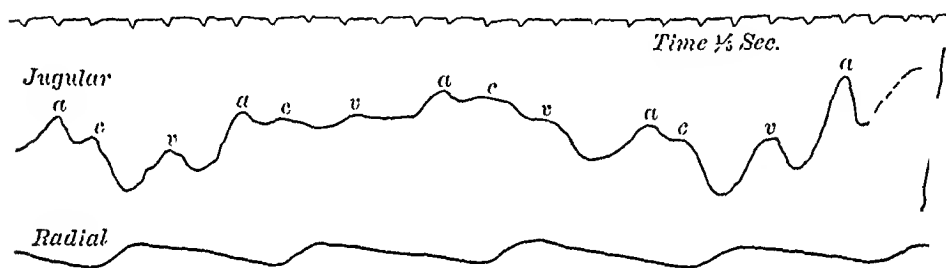


FIG. 8

CASE II.—*Heart-block with Stokes-Adams Syndrome.* The patient, a Jewish grocer, aged thirty years, is married, but has no children. He uses little alcohol, takes one cup of coffee, smokes seven cigarettes a day, and works long hours without out-of-door exercise. The past history includes scarlatina, measles, and probable pneumonia. There has been no serious illness since childhood, and no rheumatism or chorea.

The present illness goes back twelve years, at which time there were two or three syncopal attacks. These were repeated seven, five, and one year ago, and also two weeks before the present observation. These attacks have never been seen by a physician, but the patient says his face is at first flushed, then pale, and, as the paroxysm subsides, he feels his heart begin to beat hard. The trouble was first discovered six years ago, when his physician found an intermittent pulse, the rate 19 to 24, and the heart sounds at most 48. The patient considered himself perfectly well, and said his heart had been that way the past ten years. For a year and a half there has been oedema of the right leg. There has been no dyspnoea.

*Physical Examination*, January 3, 1908. The weight is 133½ pounds. The skin is rather pale, but the mucous membranes are of good color. The heart is moderately enlarged, the impulse one-half inch beyond the nipple line, and broad and lifting. No displacement by change of position is noted. There is a harsh apical and a slighter basic systolic murmur. The rate is 24, with occasionally an extrasystole. The arteries are slightly thickened. The arterial pressure is, systolic, 200; diastolic, 100. There are two or three jugular pulsations to each carotid. No auricular sounds can be heard. The right leg and thigh show tense oedema, probably from thrombosis of the femoral vein.

*Later History*—January 23, 1909. No faints have occurred during the past year. The heart is as before, except that no extrasystoles are made out. There are no intermediate sounds. The tracings (Fig. 9) were made on this date.

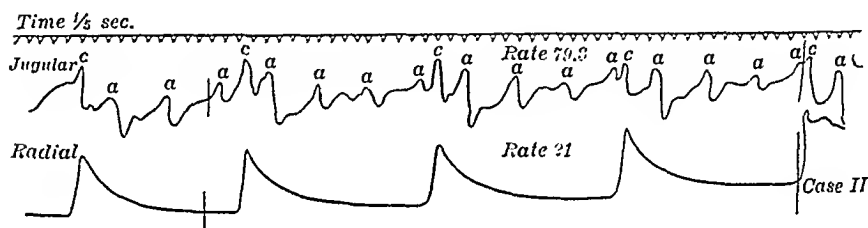


FIG. 9

*Analysis of the Tracings.* These show an auricular rate of 79.3; a ventricular of 21; a complete dissociation. However, the close approximation to a 4 to 1 rhythm is confusing, and a partial association in this ratio can be eliminated only by careful analysis. This close numerical relationship between auricular and ventricular rate in complete dissociation has several times come to my notice, and may easily be a source of error in the interpretation of a tracing. Figs. 4 and 5 of Case I, as well as the tracing from Case III (Fig. 10), also illustrate this point. The progressive diminution of the negative phase of each successive auricular wave occurring during a ventricular cycle, illustrating the degree of ventricular filling, is well shown. The history of bradycardia for sixteen years, of fainting attacks, beginning twelve years back, and continuing with remissions of one, two, four, and five years' duration, is unusual and gives peculiar interest to the future progress of the case.

*CASE III.—Heart-block without Stokes-Adams Syndrome.* The patient is a man, aged fifty-four years, a bookkeeper, whose father died at seventy-one of apoplexy. There is no history of alcoholism. He uses little tobacco or coffee, and was never ill until three and a half years ago.

Beginning three and a half years ago the patient suffered severe

abdominal pain after eating, became anemic, and six months later had severe melena. A stomach specialist diagnosticated duodenal ulcer from enteroptosis, and applied an abdominal belt, with relief of symptoms until December 8, 1908. At this time he began to suffer from epigastric pain and shortness of breath. His physician discovered a pulse of 35 and an enlarged liver, due to heart insufficiency. No one knows how long this bradycardia had existed, but it has been continuous since December 8, 1908; the rate varying between 33 and 41. With this has been dyspnoea and general incapacity for effort, so that the patient is carried upstairs. There has never been a single syncope or convulsion. Treatment with digitalis, convallaria, and strychnine has been without effect.

*Physical Examination*, March 2, 1909. The weight is  $125\frac{3}{4}$  pounds, the height five feet two and one-half inches. There is pallor with slight cyanosis. The heart is somewhat enlarged downward and outward; the rate 34. The jugular vein shows a more frequent rhythm, judged to be about a 3 to 1, and apparently dissociated. There is no distinct heart murmur, but the first sound is

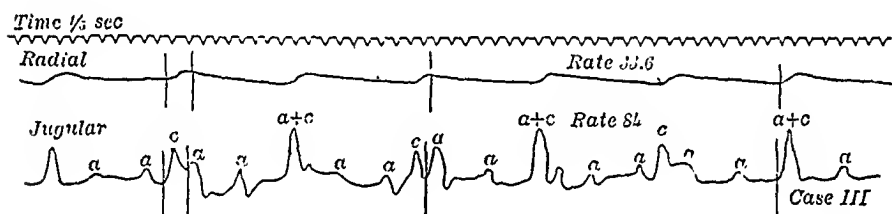


FIG. 10

low pitched and the second sounds are distant. The arteries do not seem thickened. The arterial pressure is, systolic, 240; diastolic, 110. The lungs are clear. The abdomen shows nothing abnormal. The liver is not enlarged, nor is there œdema. The hemoglobin is 95 per cent. The tracings (Fig. 10) were made March 2.

*Later History.* April 27, 1909. The patient writes from the country that for several weeks the pulse had been 72, and he had been feeling perfectly well until the onset of hot weather, when his pulse rate again fell to 40 and he was less comfortable. It is reasonable to infer a renewal of *a-v* association with subsequent lapse into a condition of partial or complete dissociation. This may be considered a probable instance of the occasional temporary character of heart-block.

*Analysis of Tracings.* These show a very remarkable *a-v* "dissociated association," the parallel of which we have yet to discover. The auricular rate is 84, the ventricular, 33.6; or an exact 5 to 2 rhythm. Furthermore, each alternate ventricular contraction is coincident with an auricular. This fact obtains throughout all the considerable length of tracings made, and so cannot be regarded

as a mere accident of the moment. Such a phenomenon suggests the possibility of a rhythmic  $\alpha$ - $\nu$  association of a type not yet worked out and one the existence of which must be established by further observations before its etiology can be taken into account.

The prolonged condition of bradycardia and heart-block without convulsions or faints is the feature of Case III most deserving of emphasis.

I gratefully acknowledge the assistance of Dr. Theodore C. Janeway at every part of this study: in supplying the clinical material and polygraph, in the labor of recording the tracings, and in the many valuable suggestions he has given.

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## THE PHYSIOLOGY AND PATHOLOGY OF CREATININE AND CREATINE.

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OUR knowledge of creatinine and creatine has reached a point where a résumé can with advantage be given to the clinician, and it is the purpose of this paper to present briefly the present conception of this subject.

With the appearance, in 1904, of the Folin<sup>1</sup> method for the accurate determination of both creatinine and creatine the investigation of the relation of these two bodies to metabolism received a great impetus. In his lecture on "Chemical Problems in Hospital Practice," delivered before the Harvey Society nearly two years ago, Professor Folin<sup>2</sup> made this statement: "I venture to predict that we shall learn more concerning the abnormal or subnormal metabolism of the sick on the basis of creatinine and creatine determinations alone than could be learned in another thirty years by means of the nitrogen determinations of the past." The importance and widespread interest in this question is again exemplified by the admirable paper of Professor Mendel,<sup>3</sup> given in the symposium on this subject before the various allied societies at their annual meeting in Baltimore last year.

**THE PHYSIOLOGICAL ELIMINATION OF CREATININE.** Folin<sup>4</sup> was the first investigator to point out that the amount of creatinine excreted in the urine by a normal individual is quite independent of either the amount of protein in the food or of the total nitrogen

<sup>1</sup> Ztschr. f. phys. Chem., 1904, xli, 233.

<sup>2</sup> Jour. Amer. Med. Assoc., 1908, i, 1391.

<sup>3</sup> Science, 1909, xxix, 584.

<sup>4</sup> Amer. Jour. Phys., 1905, xiii, 46. See also Amer. Jour. Insan., 1904, lx, 699, and lxi, 299,

in the urine, the amount excreted from day to day being practically constant for each individual (presumably in the same physical condition). The constancy of this creatinine excretion has been fully confirmed by van Hoogenhuyze and Verploegh,<sup>5</sup> Klercker,<sup>6</sup> Closson,<sup>7</sup> and Shaffer.<sup>8</sup> Shaffer<sup>9</sup> has further observed just as great uniformity in the hourly excretion of creatinine as is found in the daily excretion. Even very great diuresis has no effect on this hourly elimination. A great increase or decrease in the amount of protein ingested at a single meal, resulting in marked change in the amount of total nitrogen excreted per hour, is also without effect upon the hourly excretion of creatinine. Furthermore, experiments by both van Hoogenhuyze and Verploegh,<sup>10</sup> and Shaffer have shown that neither increased nor decreased muscular activity uncomplicated by other factors has any effect upon the creatinine elimination. Such results indicate that the regularity of excretion of creatinine is to be explained by a regularity of formation, and not merely by a regular kidney secretion.

While the creatinine excretion is practically constant from day to day for each healthy individual, different persons excrete different amounts, and Folin pointed out that "the chief factor determining the amount of creatinine eliminated appears to be the weight of the person." He further noted that the fatter the subject, the less creatinine is excreted per kilo of body weight and concluded from this that the amount of creatinine excreted depends primarily upon the mass of active protoplasmic tissue. This, however, is not the only factor of influence, and on account of the complexity of the subject it is difficult to point out the factors involved. This question was discussed at length by Benedict and me<sup>11</sup> from the study of a large number of cases in the Connecticut Hospital for the Insane. In the case of women, the same investigators found that the creatinine excreted was, in general, much lower than that of men, doubtless due to their poorer muscular development. Here the creatinine-forming process is less active, and there is, at the same time, a lower muscular efficiency.

The significant physiological fact to be borne in mind in regard to creatinine is the absolute constancy of its elimination, different for different individuals, but wholly independent of quantitative changes in the amount of nitrogen excreted, thus pointing conclusively to its endogenous origin. As Folin has indicated, creatinine is by far the most reliable index as to the amount of a certain kind of true tissue katabolism occurring daily in any given individual. It has been found convenient to express the daily creatinine elimina-

<sup>5</sup> Ztschr. f. phys. Chem., 1905, xlv, 415.

<sup>6</sup> Beitr. z. chem. Phys. u. Path., 1906, viii, 59.

<sup>7</sup> Amer. Jour. Phys., 1906, xvi, 252.

<sup>8</sup> Ibid., 1908, xxii, 445.

<sup>11</sup> Amer. Jour. Phys., 1907, xviii, 377.

<sup>9</sup> Ibid., 1908, xxiii, 1.

<sup>10</sup> Ztschr. f. phys. Chem., 1908, lvi, 161.



tion in milligrams of creatinine nitrogen per kilo of body weight, and this has been called the creatinine co-efficient. For a strictly normal individual, this co-efficient is between 7 and 11 milligrams of creatinine-nitrogen.

THE ELIMINATION OF CREATININE IN PATHOLOGICAL CONDITIONS. That the creatinine elimination is affected by different pathological conditions has been shown by a number of investigators. In general, it may be stated that fevers produce an increase in its elimination, while a decrease is observed in a large number of other pathological states.

The effect of fever on the creatinine output has been studied by Leathes,<sup>12</sup> van Hoogenhuyze and Verploegh, Shaffer, and Klercker.<sup>13</sup> The rise in body temperature was found to be accompanied by an increased creatinine elimination. Van Hoogenhuyze and Verploegh noted the maximum creatinine excretion at the same time, or within a few hours of the highest temperature. In a study of such fevers as pneumonia, erysipelas, and typhoid, Klercker observed that during a long course of fever the height of the creatinine elimination decreases and may finally become considerably subnormal. After a short course of fever an increase may be found even during convalescence.

In an extended study of seven insane patients, van Hoogenhuyze and Verploegh observed variations in the creatinine elimination during periods of exultation and depression, there being an increase during the former and a decrease during the latter. They also observed an increase under the effects of stimulation with alcohol, syrup of cola, and strychnine, and a decrease following potassium bromide and absolute rest.

A low creatinine elimination has been found associated with a large number of abnormal conditions, especially those accompanied by muscular weakness. Benedict and I observed a creatinine co-efficient as low as 2 in two very old, decrepit women. In very young infants, Amberg and Morrill<sup>14</sup> found the co-efficient between 1.5 and 2.6, figures which one would expect from the small bulk of of muscular tissue. Funaro<sup>15</sup> obtained similar results.

In patients suffering from exophthalmic goitre Shaffer observed a very low excretion of creatinine, even though the total endogenous metabolism was above the normal, as shown by a rapid loss of weight and by emaciation. He concluded that creatinine was not a product of total tissue katabolism, but rather of certain normal cell processes, which in many diseased conditions may be extremely sluggish in their intensity. Forschbach<sup>16</sup> likewise observed a low creatinine output in cases of exophthalmic goitre. In two cases of myelogenous leukemia this author noted a low creatinine elimina-

<sup>12</sup> Jour. Phys., 1907, xxxv, 205.

<sup>14</sup> Jour. Biol. Chem., 1907, iii, 311.

<sup>16</sup> Arch. f. exp. Path. u. Pharm., 1907, lviii, 112.

<sup>13</sup> Ztschr. f. klin. Med., 1909, lxxviii, 22.

<sup>15</sup> Biochem. Ztschr., 1908, x, 467.

tion, and in one case of lymphatic leukemia Shaffer reported a similar result. Mellanby<sup>17</sup> has recorded a diminished elimination of creatinine in disease of the liver, especially carcinoma.

Spriggs<sup>18</sup> reported a very low creatinine excretion in two cases of muscular dystrophy (co-efficients 2.2 and 4.0), and in one case of amyotonia congenita (co-efficient 1.9). He has also observed a much diminished elimination of creatinine in a case of pseudo-hypertrophic muscular dystrophy.<sup>19</sup> Levene and Kristeller<sup>20</sup> found very low creatinine co-efficients in four cases of muscular dystrophy, the co-efficient obtained from the average of six observations on one patient, aged seventeen years, being 1.5.

The effect of fasting on the creatinine elimination has been studied by van Hoogenhuyze and Verploegh, Benedict,<sup>21</sup> Benedict and Diefendorf,<sup>22</sup> and Cathcart.<sup>23</sup> In general, a moderate diminution in the creatinine has been noted during the progress of the fast. Similar results have been obtained on animals by Underhill and Kleiner<sup>24</sup> and also in experiments by Mendel and me.<sup>25</sup>

Changes have been noted in the creatinine elimination of experimental animals under the influence of various poisons, especially those which tend to produce a degeneration of liver tissue, such as potassium cyanide, hydrazine, phosphorus, amyl alcohol, and chromates. Such experiments have been performed by Loewy, Wolf and Osterberg,<sup>26</sup> Richards and Wallace,<sup>27</sup> Underhill and Kleiner, Lusk,<sup>28</sup> and Lefmann.<sup>29</sup>

**CREATININE IN MUSCLE.** The recent papers of Grindley and Woods,<sup>30</sup> Mellanby, and Mendel and Leavenworth<sup>31</sup> appear conclusive that creatinine is not present preformed in the muscular tissue and hence our consideration of this compound is wholly confined to its elimination in the urine.

**THE ELIMINATION OF CREATINE.** In his original discussion of the subject Folin pointed out that although creatine is normally absent from urine, occasionally small amounts can be found. Benedict first noted that during inanition (experiments on a professional faster) considerable quantities of creatine appear in the urine, and subsequently in collaboration with Diefendorf confirmed this on a fasting woman. Independently, Cathcart observed this elimination of creatine during inanition. In fasting experiments which he conducted on rabbits, Dorner<sup>32</sup> also noted the

<sup>17</sup> Jour. Phys., 1908, xxxvi, 447.

<sup>18</sup> Biochem. Jour., 1907, ii, 206.

<sup>19</sup> Carnegie Inst., Washington, 1907, Pub. No. 77, 386.

<sup>20</sup> Amer. Jour. Phys., 1907, xviii, 362.

<sup>21</sup> Jour. Phys., 1907, xxxv, 500; also Biochem. Ztschr., 1907, vi, 133.

<sup>22</sup> Jour. Biol. Chem., 1908, iv, 165.

<sup>23</sup> Biochem. Ztschr., 1908, viii, 123.

<sup>24</sup> Amer. Jour. Phys., 1907, xix, 461.

<sup>25</sup> Jour. Biol. Chem., 1907, ii, 309.

<sup>26</sup> Ztschr. f. phys. Chem., 1907, lii, 225.

<sup>18</sup> Quart. Jour. Med., 1907, i, 63.

<sup>20</sup> Amer. Jour. Phys., 1909, xxi, 45.

<sup>21</sup> 77, 386.

<sup>22</sup> Jour. Phys., 1907, xxxv, 500; also Biochem. Ztschr., 1907, vi, 133.

<sup>23</sup> Unpublished results.

<sup>24</sup> Jour. Biol. Chem., 1908, iv, 179.

<sup>25</sup> Ztschr. f. phys. Chem., 1908, lvii, 476.

<sup>26</sup> Amer. Jour. Phys., 1908, xxi, 100.

appearance of creatine; while in similar experiments on dogs, Underhill and Kleiner, and Richards and Wallace obtained the same results. In an experiment made by Mendel and me on a fasting dog, it was found that after creatine had been continuously excreted for some time, it could be made to disappear by a practically pure carbohydrate diet.

Benedict and I<sup>33</sup> were the first workers to report the elimination of creatine in a large number of individuals. In general, the quantity found was not large; though in one case the amount of creatine was greater than creatinine. The presence of this creatine in these cases may, perhaps, be generally explained as due to malnutrition.

Both Mellanby and van Hoogenhuyze and Verploegh have reported observations on patients suffering with carcinoma of the liver. Here the creatine elimination is very high, often a gram and a half per day. The latter investigators have found creatine almost absent in carcinoma of the stomach, thus pointing to some probable lack of liver function in the first instance.

In two cases of diabetes, Shaffer reports a considerable elimination of creatine, but in a measure, at least, this finds explanation in the meat diet. I have noted the same result in several cases which I have had occasion to examine. Shaffer has reported a considerable elimination of creatine in exophthalmic goitre. During the postpartum resolution of the uterus in women he has observed a marked elimination of creatine. This has also been noted by Murlin<sup>34</sup> in dogs. A considerable elimination of creatine during typhoid fever has been reported by Shaffer, and from a study of fevers Klercker concludes that sooner or later after the onset of fever, creatine is eliminated, a condition which lasts for a longer or shorter time, often to convalescence. Levene and Kristeller report the elimination of creatine, especially in their cases of muscular dystrophy.

Loewy, Wolf, and Osterberg, and Richards and Wallace, in their work with potassium cyanide, found the creatine elimination in dogs to be increased. Underhill and Kleiner obtained the same results with hydrazine, and likewise Lefmann from chromate poisoning.

**CREATINE IN MUSCLE.** According to Urano,<sup>35</sup> muscle tissue contains about 0.4 per cent. of creatine, and from this it has been calculated that a man weighing 60 kilos would have from 90 to 100 grams of creatine stored up in his muscle. In this connection, it is of interest that, according to Urano, the creatine of the muscle appears to be held in some non-diffusible form in the contractile tissue, and is only released when the integrity of the muscle

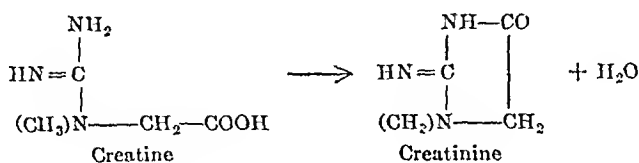
<sup>33</sup> Amer. Jour. Phys., 1907, xviii, 407.

<sup>34</sup> Ibid., 1909, xxiii, xxxi.

<sup>35</sup> Beitr. z. chem. Phys. u. Pathol., 1907, ix, 104.

bundle is impaired. The experiments of Mellanby indicate that the performance of muscular work leaves the creatine unaffected. Saiki<sup>36</sup> has demonstrated the presence of creatine in non-striated mammalian muscle, though here the quantity is much smaller, less than 0.1 per cent. It is not found, however, in invertebrate muscle.

RELATIONSHIP BETWEEN CREATININE AND CREATINE. Since creatine can be easily converted into creatinine under the hydrolytic action of weak acids, it was quite logical for the physiologist to assume some genetic relation between these compounds in the living body.



From this point of view, creatine was looked upon as a product of protein metabolism in muscle, easily converted into the "anhydride" creatinine and thus eliminated in the urine. However, the attempt to connect the excreted creatinine with tissue creatine brought to light an apparent independence of these compounds in metabolism. Ingestion of creatinine results in an increased creatinine elimination, but when creatine is fed to man or animals Folin,<sup>37</sup> Klercker,<sup>38</sup> van Hoogenhuyze and Verploegh, and Lefmann have all found that the creatinine content of the urine is only slightly altered if at all; nor is the creatine itself eliminated. Observations by Lefmann also uphold this for creatine introduced parenterally. The fact that ingested creatine is apparently not changed to creatinine in the body, together with the appearance of creatine in the urine during inanition and also certain other pathological conditions, led Folin, Benedict, and Klercker to question any biological relationship between these two compounds. The unique appearance of creatine under these circumstances must be borne in mind whenever this substance is found accompanying abnormal conditions attended by inadequate nutrition. In practically every such case it is reasonable to ascribe the source to the creatine of the muscle. As was stated above, creatine is excreted in acute fevers and various manifestations in which there is a rapid loss of muscle proteins. The creatine elimination is likewise marked in the urine of women during the first week post partum, when resolution of the uterus is taking place. However, in the majority of the conditions in which creatine is eliminated the creatinine excretion is abnormal and, as a rule, subnormal. This seems to be especially noteworthy in cases of muscular dystrophy and carcinoma of the liver. The evidence

<sup>36</sup> Jour. Biol. Chem., 1908, iv, 483.

<sup>38</sup> Biochem. Ztschr., 1907, iii, 43.

<sup>37</sup> Festschrift f. Olof Hammarsten, 1906, 111.

presented by Mellanby, van Hoogenhuyze and Verploegh, and Lefmann, all point to a possible liver function in creatine and creatinine metabolism.

By an elaborate investigation of the behavior of these compounds during autolysis, Gottlieb and Stangassinger<sup>39</sup> have concluded that they can undergo a series of enzymatic transformations in the body, the more important of which are that, creatine can be formed in the autolysis of muscles and other organs, that pre-formed or added creatine can be converted by enzymatic means into creatinine during autolysis, and further, that both of these compounds may be destroyed by appropriate enzymes, creatase and creatinase. This was disputed by Mellanby, but after a repetition of the above work van Hoogenhuyze and Verploegh, Rothmann,<sup>40</sup> and Lefmann, all maintain the essential importance of endo-enzymes in the metabolism of the compounds under discussion. Such being the case, the liver is very probably the organ in the body most concerned in this action, especially in the formation of creatinine. Furthermore, it may be that when the tissues are drawn upon for supplies, as in hunger or cachexia, the creatine liberated by the disintegrating muscle now escapes destruction, owing to the lowered efficiency of some katabolic organ, such as the liver, and is eliminated as such.

At the present time it is impossible to formulate any hypothesis of creatine and creatinine metabolism which will correspond with all the data at hand. Creatinine is, however, very evidently a product of normal katabolism, possibly of muscle tissue. It is formed as the result of certain normal cell processes and is an index of the amount of a certain kind of true tissue metabolism. Creatine, on the other hand, is formed as the result of certain abnormal processes, and is, perhaps, an index of the amount of protein destruction. In one case the creatinine is apparently the result of the ordinary wear and tear, while in the other conditions, in which the protein is used to supply abnormal demands made upon it (energy, etc.), creatine is liberated by the disintegrating tissue. The experiments of Mendel and myself, in which carbohydrate was found to cause the urinary creatine of a fasting dog to disappear, harmonizes with this view. This hypothesis would explain why, in pathological cases, the total creatinine (creatinine + creatine) is not constant, though generally in the cases in which creatine is eliminated creatinine is diminished. (In fevers, the creatinine elimination is increased, due possibly to the high temperature.) Flesh destruction may be rapid, as in advanced carcinoma of the liver. In the tissues where this abnormal katabolism is taking place, creatine would result, while creatinine would be formed by the tissues

<sup>39</sup> Ztschr. f. physiol. Chem., 1907, lli, 1; *ibid.*, 1908, lv, 322; and Stangassinger, *ibid.*, 1908, lv, 295.

<sup>40</sup> *Ibid.*, 1908, lvii, 131.

which were functioning normally. If the tissue destruction were great, the creatinine would necessarily be low, and, on the other hand, the creatine would be high with a high total. According to the above idea creatinine and creatine would be two phases in the katabolism of some one substance, the one a product of normal katabolism, the other of abnormal katabolism.

Many objections can be offered to such an hypothesis as the foregoing, but nevertheless it corresponds with much of the data at hand, and furthermore, aids in the interpretation of the results from a clinical standpoint.

**THE METHOD OF DETERMINING CREATININE AND CREATINE.** Inasmuch as the impetus for the recent work on creatinine and creatine has been due to the development of a satisfactory method for their accurate determination by Folin, a few statements can with advantage be made in regard to the method. This method is based upon the characteristic property possessed by creatinine of yielding a certain definite color reaction with picric acid in alkaline solution, the Jaffé color test. When properly diluted, the color corresponds almost exactly with  $\frac{N}{2}$  potassium bichromate solution which is used as a standard. By means of a good colorimeter, such as the Duboscq, the quantity of creatinine can be estimated with great accuracy. For the determination of creatine, Folin originally recommended heating 10 c.c. of urine with an equal volume of normal hydrochloric acid on the water bath for three hours to convert any creatine to creatinine. The colorimetric estimation would then give the total creatinine, and by subtracting the preformed creatinine from the total, the creatine would be obtained in terms of creatinine. While working with Benedict,<sup>41</sup> I found that this hydrolytic action by which the creatine was changed to creatinine could be completed in one-half hour in an autoclave at 117° to 120° C., and this is the method of conversion now generally employed.

**SUMMARY.** The significant physiological fact to be borne in mind in regard to creatinine, is the absolute constancy of its elimination, different for different individuals, but wholly independent of the volume of the urine and the amount of nitrogen excreted. Creatinine is an index of some special process of normal metabolism taking place largely, if not entirely, in the muscles. The intensity of this process appears to be associated with the muscular strength of the individual. In pathological conditions, the creatinine excretion is usually low. From this point of view, the creatinine output may be looked upon, at least to a certain extent, as an index of the physical condition of the patient. The creatinine elimination appears to be especially low in conditions associated with muscular weakness or inefficiency. It is, however, slightly increased in acute fevers and here does not run parallel with the muscular strength.

<sup>41</sup> Amer. Jour. Phys., 1907, xviii, 397.

In diseases in which the creatinine output is low, creatine is generally excreted. Creatine is not normally present in the urine, and its excretion may be regarded as pathological. Furthermore, it is usually found to be associated with a loss of muscle protein, thus indicating that the source of the endogenous urinary creatine is the creatine of muscle tissue.

## A SKIN REACTION IN CARCINOMA FROM THE SUBCUTANEOUS INJECTION OF HUMAN RED BLOOD CELLS.

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CLINICAL and experimental investigations have shown that in the growth and breaking down of malignant tumors substances are formed and set free which are very poisonous to the red cells of the blood, and which probably cause the anemia and cachexia of malignant disease. Although the nature of most of these poisonous substances has not yet been determined, some of them are known to belong to the class of lysins.

The knowledge that extracts of malignant tumors have marked hemolytic qualities naturally led to the search for hemolysins in the serum of animals and of man affected with malignant disease. If the blood serum of patients suffering from malignant disease contained hemolysins, while that of normal individuals or of those suffering from other diseases did not, then we would have at our command a method of value for the diagnosis of malignant disease. Crile, Weil, Pesskind, Blumgarten, Epstein and Ottenberg, Kelling, Kullman, and many others have made studies of the blood serum of patients, in order to determine whether there was anything characteristic in the blood of individuals with carcinoma. Crile claimed that in the early stages of carcinoma the blood serum was markedly hemolytic, and that as the disease advanced, the hemolytic properties of the serum disappeared. The other investigators substantiated Crile's claim that a number of the serums from carcinoma patients possessed hemolytic qualities, but they were able to find hemolytic serums only in a much smaller percentage of patients than did the first-named investigator. All agree that hemolysins for human red blood cells are present in 50 to 60 per cent. of the patients, although hemolysins exist in the serum of many other dis-

eased individuals. The hope that the hemolytic test might prove of clinical value in the diagnosis of carcinoma has thus far been proved futile.

Weil, who was one of the earliest to investigate the subject, and who has published careful and critical studies of hemolysis in malignant disease, comes to the conclusion that it is possible that "something of value may eventually come of the use of this method in human disease, but that it will have to come with a refinement of method which will correspond to the complexity of the factors involved."

The hemolytic tests are made by mixing the serum of the patient with stated quantities of suspensions of washed human red blood cells from normal individuals. The tubes are kept in the thermostat for a number of hours, and the presence or absence of hemolysis is determined by the appearance of the supernatant fluid after the red cells have settled. If hemolysis has taken place, the fluid is colored pink or red by the hemoglobin which has been set free. By this method, the degree and presence of hemolysis is determined by the amount of laking of the red cells. The hemoglobin is therefore the indicator. The test-tube reaction gives no evidence of other substances which have been liberated. A small amount of hemolysin in the serum that is being tested may be insufficient to hemolyze enough cells to produce a coloration of the supernatant fluid appreciable to the eye.

It occurred to one of us<sup>1</sup> that it might be possible to gain a better knowledge of the hemolytic properties of the serum of human beings with malignant disease if red cells from a normal individual were brought into contact with the serum of patients *in vivo*—that is if the cells were injected under the skin of the patients.

Theoretically there might be certain advantages in such a method. If normal red blood cells are injected under the skin of a patient whose serum is hemolytic, fresh quantities of hemolysin would be continually brought to the cells by the circulating blood and lymph, and therefore—even if the amount of the hemolysin in the blood of the patient was very small—the injected cells might nevertheless be hemolyzed. Every organic substance which was liberated by the destruction of the injected red cells would enter the tissues and there have its effect. The hemoglobin and other substances which had been set free might cause a local change in the tissues at the site of the injection. If blood cells are injected under the skin of a normal individual, they are broken up and carried off by the body cells and fluids; the condition of affairs under the skin of a patient whose blood serum contains free hemolysins would be an entirely different one because a different process was taking place.

These theoretical considerations led one of us<sup>2</sup> to suggest that

<sup>1</sup> Ebsberg, Jour. Amer. Med. Assoc., March 27, 1909.

<sup>2</sup> Ibid.



injections of washed human red blood cells from normal individuals should be made under the skin of normal and of diseased individuals, in order to determine whether a local reaction was produced, and if so, if there was anything characteristic in the appearance of the skin at the site of the injection in patients who suffered from carcinoma. As we shall report in what follows, a decided local reaction was observed in a large percentage of the patients with malignant disease, while no reaction was observed in a large percentage of normal individuals or of those with other diseases.

**TECHNIQUE.** The blood is obtained in the following manner: Into an ordinary aspirating syringe of 10 to 15 c.c. capacity a glass bead about the size of a split pea is placed, and the syringe and needle are boiled in normal saline solution. The anterior aspect of the elbow of the individual whose vein is to be aspirated is carefully cleaned with soap and water, alcohol and ether, and a vein made prominent by tying a bandage around the arm. Under proper aseptic precautions the vein is punctured and 5 to 10 c.c. of blood is aspirated into the cooled syringe. The needle is then removed from the syringe, the end of the latter covered with a piece of sterile gauze, and the syringe shaken for ten minutes. After the blood has been defibrinated in this manner, about 1 c.c. is expressed into each of a number of sterile test-tubes that fit into an ordinary centrifuge, and that have been previously half filled with sterile normal salt solution. The usual bacteriological technique (passing the ends of the test-tubes through the flame, etc.) is employed to keep the contents of the tubes sterile.<sup>3</sup> The tubes are now placed in the centrifuge for ten minutes. The clear supernatant fluid is then carefully poured off from each tube under the proper precautions to prevent infection. Fresh sterile salt solution is added, the tubes are gently shaken to mix the blood with the solution, and the tubes are again centrifuged for ten minutes. The same process is repeated a third time. Then, after the supernatant fluid has been poured off, four times as much salt solution as there are cells by volume is added. Thus, approximately, a 20 per cent. suspension of washed red blood cells has been obtained. The tubes are kept in the ice chest for 24 to 48 hours, and are then ready for use. Any tubes in which there is the slightest amount of laking must not be used. If careful technique has been employed, the red cell suspension will often be free from laking for three or four days.<sup>4</sup>

It is important to select the proper individual from whom the blood is to be obtained. Tuberculosis and syphilis must be excluded, the patient must not only be free from any evidence of disease, but must not have been recently ill, nor have received any injury, must not have had even the slightest operation, and must not have

<sup>3</sup> In our entire series there was not a single case of infection. Cultures were made from a number of the tubes; they were always found to be sterile.

<sup>4</sup> We have been unable to keep the suspension free from laking for more than five days.



FIG. 1.—The skin lesion in a patient with carcinoma of the stomach eight hours after the injection.





FIG. 2.—The skin lesion in a patient with carcinoma of the breast about seven hours after the injection.



rectly had an anesthetic. The blood of individuals who have had any of these conditions is unfit for injection purposes. The blood can, however, be taken from a patient during the early stages of ether anesthesia. We have found that the most satisfactory blood is that obtained from small children, and in the hospital we have usually obtained it from little patients who were to be operated upon for hernia.

We have given injections of the blood of animals whose cells are known to be resistant to hemolysis by normal human serum, but the results obtained were not satisfactory. We have also made injections of mixed cells from several individuals, but we soon found that there was no advantage to be gained from blood mixtures. We have, finally, used suspensions of various strengths for injection purposes, but we have found that the 20 per cent. suspension gave the best results.

*The Method of Injection.* A hypodermic syringe which has been boiled in normal saline solution and cooled is filled with the blood mixture. For this purpose the tube which contains the blood is thoroughly shaken, and some of the mixture is poured into a watch crystal which has been sterilized by boiling in normal salt solution. From this watch crystal the blood is drawn up into the syringe. The skin on the anterior aspect of the forearm of the patient is cleansed with alcohol, and 5 minims of the suspension is injected in an upward direction under the skin, at a spot where there are no visible veins. The injection raises the skin, but the elevation disappears after a few minutes. The injection is not painful, and requires but a moment. Care must be taken that the blood is injected under and not into the skin.<sup>5</sup>

**THE REACTION.** The reaction begins to show itself in about five hours after the injection; it gradually increases in intensity until it has reached its height in six to eight hours. It may appear sooner than the time stated, even as early as two hours after the injection, or may require eight hours before it becomes evident. When fully developed, the reaction appears as a somewhat irregular oval area with a well-defined margin measuring from 1 x 2 to 3 x 5 cm. The margin is often surrounded by a whitish areola. The color of the lesion varies from a brownish red to a maroon, with, rarely, a bluish tinge (Figs. 1 and 2). The lesion is distinctly raised from the surrounding skin surface. At times this elevation is so slight that careful examination in good daylight is necessary to recognize it. The raised area has a slightly boggy feeling, as if there were a subcutaneous exudation, and it is often somewhat tender.<sup>6</sup>

<sup>5</sup> Some intracutaneous and cutaneous tests were attempted after the method of von Pirquet, but without success.

<sup>6</sup> Up to the present time only three specimens of skin from patients who presented the characteristic lesion have been examined microscopically. We have to thank Dr. Mandelbaum, director of the Pathological Laboratory of Mt. Sinai Hospital, and Dr. Buerger,

The lesion may appear slowly or rapidly, it may remain stationary for several hours, and fade quickly or gradually. Sometimes it has entirely disappeared six hours after the injection, at other times it begins to fade only after ten to twelve hours. When the lesion has disappeared, there remains behind a flat yellowish or greenish discoloration such as is left by any small ecchymosis (Fig. 3). In those cases in which the characteristic lesion does not appear the skin either presents no change except the needle puncture; or a small flat area of varying color; rarely, the skin is raised, but of normal color. The typical color and elevation being best seen in daylight, it is advisable to make the injection in the morning. We have usually given the injections between nine and ten in the morning and have completed our observations at six in the evening.

**RESULTS.** Up to the present time we have given 684 injections to 432 patients. For purposes of classification, we have divided the cases into the following groups (see Table I):

1. *Patients with carcinoma*, in whom the diagnosis was positive as proved by operation, autopsy, pathological examination; and patients in whom the diagnosis of malignant disease was rendered very probable by the presence of a tumor and the other symptoms which are characteristic of cancer.

2. *Patients in whom the absence of malignant disease was certain.* Among these were individuals suffering from every variety of acute and chronic disease that is to be met with in a large general hospital. Among the diseases may be mentioned acute and chronic inflammatory diseases, such as pneumonia, typhoid fever, nephritis, appendicitis, cholecystitis, osteomyelitis, abscesses, tuberculosis, syphilis, pernicious anemia, leukemia, Hodgkin's disease, myeloma, glanders, benign newgrowths, acute and chronic diseases of children, etc. In this connection it is but fair to mention that some of the patients who were treated at the hospital and discharged with other diagnoses may have nevertheless suffered from malignant disease which gave no symptoms while the patients were under observation.

3. *Possible Carcinoma.* Patients in whom malignant disease was suspected but in whom no positive diagnosis could be made before the patients left the hospital.

4. *Very Advanced and Miliary Carcinoma.* Cachectic and anemic individuals with metastases and generalized malignant disease, in the last stages of carcinoma.

associate in surgical pathology, for the preparation and examination of the specimens. A large number of specimens with the proper controls will be examined and reported on in the future. It may be of interest, however, to quote the following from Dr. Buerger's report: "In a general way it may be said that the individual pictures have little in common. Specimen I shows an acute inflammatory process with marked exudation of polynuclear leukocytes" (lesion was 24 hours old); "specimen II is characterized by dissolution and disappearance of red blood cells" (8 hours old); "specimen III must be regarded as difficult of interpretation, because the hemorrhage below the skin could be considered either as injected blood or as blood extravasation due to removal of the specimen." —



FIG. 3.—The greenish discoloration (ecchymosis) twenty-four hours after the lesion had disappeared. The patient had a carcinoma of the thyroid gland.





TABLE I.

	No. of cases.	Positive reactions.	Negative reactions.	Doubtful reactions. <sup>7</sup>
Carcinoma, positive or probable . . . . .	69	62=89.9%	5=7.2%	2=2.9%
No carcinoma . . . . .	325	15=4.6%	307=94.3%	3=1.1%
Possible carcinoma . . . . .	9	7=77.8%	2=22.2%	.....
Carcinoma, advanced or miliary . . . . .	11	.....	11=100%	.....

Table I shows that a positive skin reaction was observed in 90 per cent. of the patients with carcinoma (excepting the very advanced), and that there was no reaction in 94 per cent. of the patients who were suffering from other diseases. Of the patients in whom carcinoma was suspected but could not be proved, 78 per cent. gave a positive reaction. In all of the patients with advanced malignant disease, with metastatic deposits in the various viscera or miliary carcinoma, etc., no skin reaction was observed after the injections.<sup>8</sup>

TABLE II.

Carcinoma of	No. of cases.	Positive reaction.	Negative or doubtful reaction.
Lip, palate, tongue . . . . .	3	3	0
Neck . . . . .	1	1	0
Esophagus . . . . .	5	3	2
Stomach . . . . .	22	21	1
Liver . . . . .	2	1	1
Large and small intestine . . . . .	2	2	0
Rectum . . . . .	5	4	1
Abdomen . . . . .	5	3	2
Abdomen, metastatic tumor . . . . .	3	1	2
Abdomen, miliary or multiple metastases.	7	0	7
Pancreas <sup>9</sup> . . . . .	1	0	1
Thyroid . . . . .	2	2	0
Mediastinum . . . . .	3	3	0
Lung . . . . .	1	1	0
Breast . . . . .	6	6	0
Bladder . . . . .	3	3	0
Prostate . . . . .	2	2	0
Uterus . . . . .	4	4	0
Vagina . . . . .	1	1	0
Skin . . . . .	1	1	0
Spine, metastatic tumor . . . . .	1	0	1

<sup>7</sup> These are reactions that resemble in appearance the type reaction, but not closely enough to call them definitely positive.

<sup>8</sup> We have tested patients with sarcomatous disease, but the number thus far examined has been small. Of seven patients with sarcoma, four gave a positive reaction. Of three cases of hypernephroma, one gave a positive reaction.

<sup>9</sup> Postmortem examination revealed one microscopic nest of carcinoma.

Table II gives a list of all the patients with carcinoma to whom blood injections were given, and the results obtained. In some of the patients positive reactions were obtained after the first and no skin reactions after later injections. In a small number of patients the first injection gave negative, and later injections with other blood suspensions gave positive reactions.

In the following list are the synopses of the histories of patients with no malignant disease in whom a positive reaction was obtained. The symptoms and diagnoses are abstracted from the hospital records:

Case I.—M. C., aged sixteen years; congenital growing lymphangiomas and hemangiomas of the groin and extremities. First injection, given after removal of one of the tumors, positive; four following injections, negative.

Case II.—E. J., aged forty years; gastric history of one year's duration with loss of flesh and strength. Laparotomy failed to show carcinoma or any other lesion. Four injections, all positive.

Case III.—M. J., aged forty years; parenchymatous and cystic goitre.

Case IV.—A. S., aged forty years; double parotid tumors improved under syphilitic treatment, enlarged right kidney.

Case V.—A. H., aged seventy years; enlarged prostate, cystitis, emaciation. Postmortem examination revealed generalized miliary tuberculosis. One injection positive; three negative.

Case VI.—J. A., aged forty-six years; myxoma of the shoulder, enlarged glands in the axilla not removed.

Case VII.—B. A., aged fifty years; subphrenic abscess of unknown origin; one positive, one negative reaction.

Case VIII.—M. B., aged forty years; arteriosclerosis, bloody fluid in the pleuræ, icterus; discharged improved; medical treatment.

Case IX.—I. L., aged forty-five years; emaciated; gastric symptoms; improved under treatment; diagnosis on discharge from the medical wards was gastric ulcer.

Case X.—J. G., aged seventy years; hematemesis, emaciation, anemia. Death from repeated hemorrhages. At the postmortem examination, large pyloric ulcer.

Case XI.—S. S., aged thirty-five years; emphysema and bronchitis, obscure gastric symptoms.

Case XII.—Age unknown, discharged after a short stay in the hospital with a diagnosis of chronic appendicitis. Unfortunately, the chart of this patient can not be found.

Case XIII.—F. P., age unknown; pyosalpinx, pneumonia.

Case XIV.—V. A., aged forty-four years; incipient Basedow's disease, neurasthenia.

Case XV.—V. L., aged fifty years; progressive anemia, sudden death.

General anesthesia seems to interfere with the reaction. In a

number of patients who were given a general anesthetic for purposes of examination or operation, and who had reacted positively before, the injections gave a negative result for the first few days after the anesthesia. Some days later positive reactions were again obtained. When the malignant growth has become very far advanced, positive reactions can no longer be obtained.

Our experience is too small to permit of any statements as to the significance of positive reactions after the carcinoma has been apparently radically removed. In a few patients, on the other hand, in whom the disease seemed to have been completely eradicated, less and less marked reactions were obtained as time went on; finally, no reactions at all could be obtained. In patients in whom the disease was not or only partially removed, injections gave positive results after the effects of the anesthesia or operation had worn off.

CONCLUSIONS. 1. The subcutaneous injection of human red blood cells prepared in the manner we have described is, in certain individuals, followed by a characteristic and easily recognizable local skin lesion or reaction at the site of the injection.

2. The large majority of the patients (89.9 per cent.) in whom this skin reaction was observed were suffering from carcinomatous disease.

3. The large majority of the patients (94.3 per cent.) in whom no characteristic skin lesion followed the injection were free from carcinoma.

Finally, we desire to thank the attending physicians and surgeons of the hospital for their courtesy in placing patients at our disposal, and the members of the house staff for their ever-ready aid in obtaining the clinical material and the data we required.

## REVIEWS.

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**SURGICAL DIAGNOSIS.** By EDWARD MARTIN, M.D., Professor of Clinical Surgery in the University of Pennsylvania. Pp. 772; 445 engravings and 18 colored plates. Philadelphia and New York: Lea & Febiger, 1909.

A CAREFUL reading of this work, and an equally careful comparison with other treatises on surgical diagnosis, are amply convincing as to its unusual merit and usefulness. The author has wisely emphasized the paramount importance of *early* diagnosis, and has throughout obviously borne in mind the axiom which he himself enunciates: "The simplicity and safety of surgical intervention are, as a rule, proportionate to timeliness in diagnosis." No better text could have been selected for the teachings of such a book, and it would be difficult to find anywhere in surgical literature a closer adherence to the idea of setting forth the earliest symptomatology on which diagnosis can be based, or a clearer exposition of those phenomena of surgical disease or injury so often first seen by the general practitioner.

The book opens with an excellent chapter on laboratory diagnosis by Dr. Longcope. It might have been well to describe at least the nature of "Cambridge's test," as it was thought worth while to say "the test devised by Cambridge is said to be specific for diseases of the pancreas, and is thought to be especially valuable for the diagnosis of chronic inflammation of the pancreas." The only other reference to this test is on page 526, where, under "pancreatitis," it is said "the urine gives, according to Robson and Cambridge, the pancreatic reaction which they regard as diagnostic." The additional statement that the test is not generally believed to have the value they place upon it would then have left the matter clear to the reader. Under the bacteriology of the urine the relation of rectal conditions to vesical infection might with advantage have been mentioned, though later (p. 671) chronic constipation and dysentery are included among the causes of bacteriuria. No better summary of blood conditions and examinations is to be found anywhere.

Chapter II, by Dr. Pancoast, is an admirable exposition, well illustrated, of the application of the *x*-rays in surgical diagnosis. It is to be assumed that when he says "the risks involved in the radiographic examination are now so slight that they may be practically disregarded," he means risks to the operator and not the risks of misinterpretation. The latter are still with us, and should never be

forgotten. The discussion of the use of  $x$ -rays in aneurysm, in biliary calculus, and in gastro-intestinal conditions is marked by the good sense and conservatism that are known to be characteristic of the author.

Inflammation, trauma, and tumors are considered in the next three chapters, and are dealt with in outline. The salient diagnostic points are admirably, though perhaps somewhat too concisely, summarized. The article on the skin is excellently illustrated by cuts contributed by Dr. Hartzell. Much information is packed into the dozen pages allotted to this subject, but, again, the condensation is a trifle extreme. The seeker after information about itch, for example, having been told that "diagnosis is assured on finding in an unscratched region a characteristic tunnel, and made absolute by extracting the *Sarcoptes scabiei* therefrom with a fine needle," would probably desire to know what a "characteristic tunnel" looked like, and perhaps might have the same wish as to the *Sarcoptes scabiei*. The bloodvessels, muscles, tendons, and bursæ and the bones and joints each have a chapter—and in each case an interesting and instructive one; and nervous diseases are considered in eighty-three pages by Dr. Weisenburg, in a most comprehensive and satisfactory manner. Thenceforward the divisions of the book are on topographical lines—the head, the spinal column, the upper extremity, etc.—with the exception of a good chapter on gynecological diagnosis by Dr. Anspach.

While the excellent plan followed throughout the book in describing the duration of symptoms or conditions (of giving approximate times, that is, minutes, hours, days, etc., instead of using vaguer chronological adjectives) is much to be commended, occasionally it might lead to error. For instance, in describing the diagnostic features of extradural hemorrhage following trauma, Professor Martin mentions (p. 226) "an interval of freedom from symptoms (hours) followed by violent headache." While this is usually true, there are many cases in which the interval could be expressed only in fractions of an hour, or in minutes, and the unqualified use of "hours" might therefore be misleading. The general subject of cranial and cerebral trauma is, however, admirably treated, and in a most clear and accurate manner.

The fractures of the extremities are illustrated by  $x$ -ray drawings by Dr. Pancoast, from negatives made chiefly at the University Hospital, Philadelphia. They constitute the most complete series of skiagrams of fractures yet published in a surgical text-book. The legends beneath them have been prepared with unusual care, and, taken in conjunction with the accompanying instructive descriptions.—in the text—of symptoms and deformities, add greatly to the usefulness of this valuable section. Equally satisfactory are the chapters on the abdomen and on the genito-urinary organs. The synopsis of the differential diagnosis of intra-abdominal swellings

(pp. 490 to 500) is not excelled anywhere, and the articles on cystitis, vesical and renal calculus, the diseases of the kidneys and ureters, are deserving of similar commendation.

In the article on the appendix, though it covers only a little more than four pages, is to be found another excellent example of admirable condensation, of rigid exclusion of the redundant and unnecessary, and of the thoughtful enumeration of every point of absolute value clinically in reaching a diagnosis. The only omission to be noted in this connection is the failure to supplement the clinical signs by those obtained through laboratory examinations, etc. This is probably due to the fact that the blood conditions in appendicitis are described in another section (p. 20), but it would have been well to bring them together. Having regard to the student it is undesirable that the same region should be alluded to as "the ilio-costal angle" (p. 522) and the "costovertebral angle" (p. 543). When the author says "from renal pain gallstone colic is distinguished by its upward and backward radiations, absence of tenderness in the ileocecal angle, and usually by urinary findings in the latter condition," he obviously means "former" instead of "latter."

Loss of blood in ordinary hemorrhage, in purpura, in epistaxis, and in intracranial conditions is fully considered, but hemophilia might have been described with special reference to those features of the family history that are often diagnostic. Hemophilic arthritis in young persons is the only allusion to the subject that we have found, except that in the article on blood examination it is truthfully said that it should "be remembered that in hemophilia, a disease which offers great dangers to the surgeon, the coagulation time of the blood may not be decreased."

Leaving aside a few similar trifling oversights we have found, however, very few omissions of any sort, and still fewer errors. If there is a better work than this on surgical diagnosis we are not familiar with it. Believing it likely to be helpful, not only to students and practitioners, but to surgeons themselves, we feel that both author and publishers may be congratulated upon the production of a book which will be a valuable addition to every working surgical library.

W. B.

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A SYSTEM OF MEDICINE. By MANY WRITERS. Edited by SIR CLIFFORD ALLBUTT, K.C.B., Regius Professor of Physic in the University of Cambridge; and Humphry Davy Rolleston, M.D., Senior Physician to St. George's Hospital, London. Vol. V; pp. 969. London: Macmillan & Co., 1909.

As issued in its revised edition, Vol. V of Allbutt and Rolleston's *System of Medicine* is concerned with diseases of the lungs, pleuræ,

mediastinum, thymus, and the blood. The volume opens with an interesting although short account of the physical signs of the lungs and the heart, by Dr. Hector Mackenzie, which is followed by an article on artificial aërotherapeutics, by Dr. C. Theodore Williams. Drs. Goodhart and Spriggs, in discussing asthma, treat almost exclusively of primary or true spasmodic asthma, as contrasted with asthma arising as a complication of preëxisting bronchitis. They regard hay fever as often a spasmodic asthma in its purest form, and they believe the best explanation of asthma to be that which looks upon muscular spasm of the smaller bronchi as the basis of the process; while they mention Curschmann's exudative bronchiolitis, they attempt to minimize its influence, although there is excellent reason for believing that it is the essence of the process in many cases. Dr. William Ewart contributes splendid articles (over one hundred pages) on bronchitis, bronchiectasis, and bronchiolectasis, which are especially characterized by a careful classification, good clinical descriptions, and welcome details regarding treatment. He is disposed to differentiate, at least pathologically, capillary bronchitis from bronchopneumonia. Dr. A. P. Beddard has written the chapter on acute lobular pneumonia and bronchopneumonia, and has revised the chapter on lobar pneumonia originally contributed by Dr. Pye-Smith; the bacteriology and serum therapy has been entrusted to J. Eyre, who extols the value of the vaccine (bacterin) treatment of lobar pneumonia, a form of treatment but little employed as yet, but of much promise and deserving extended trial. Abscess and gangrene of the lung and newgrowths of the bronchi are adequately discussed by Dr. J. J. Perkins. Drs. Percy Kidd, W. Bulloch, and N. Bardswell contribute an excellent account of pulmonary tuberculosis (138 pages). One will find therein about all that is really known of the subject, interestingly and authoritatively set forth. Dr. Bulloch believes that infection is commonly acquired by inhalation rather than by ingestion, but he points out that the spread of the infection once acquired is mainly by way of the lymphatics. The use of tuberculin, controlled by the determination of the opsonic index, is fully set forth; perhaps too much importance is attached to the opsonic index. In addition, Dr. Kingston Fowler contributes articles on syphilis and emphysema; Drs. Rolleston and A. Latham, an article on aspergillosis; Sir Thomas Oliver, an article on pneumokoniosis, based upon large experience; and Drs. F. T. Roberts and J. J. Perkins, an article on newgrowths of the lung. The diseases of the pleura are discussed as follows: Intrapleural tension, by Dr. Samuel West; pleurisy, by Dr. Samuel Gee and T. J. Horder; pneumothorax, by Dr. D. W. Finley; and newgrowths, by Dr. F. T. Roberts and J. J. Perkins. Dr. F. T. Roberts also writes the chapters on diseases, including newgrowths, of the mediastinum, and Dr. Bosanquet the chapter on diseases of the thymus.



Somewhat more than a fourth of the book is devoted to disorders of the blood. The senior editor contributes the article on chlorosis, which is a model of scientific inquiry, clinical observation, and graceful writing. Dr. Herbert French, discussing pernicious anemia, supports Dr. William Hunter in his contention that the disease is a specific disorder consisting in hemolysis, but he is not certain that the postulated toxin is a product of the alimentary tract, preferring to believe that the nature of the toxin and its site of formation are unknown. Drs. R. Hutchison and J. C. G. Ledingham offer a really excellent discussion of the splenic anemias, and a classification satisfactory enough in view of the unsatisfactory state of our knowledge concerning the disorder, or disorders. Dr. Robert Muir contributes the article on leukemia, which is embellished by several colored plates. Dr. F. Parkes Weber writes on polycythemia and erythremia; Dr. A. E. Garrod, on enterogenous cyanosis; Sir Stephen Mackenzie, on purpura; Dr. John Thomson, on hemorrhages in the newborn; Mr. W. Johnson Smith, on scurvy; Drs. Cheadle and Poynton, on infantile scurvy; and Sir Almroth E. Wright, on hemophilia.

As a whole, the volume maintains a high level of consistent effort, of discriminating surveys of contemporaneous medical literature, and of authoritative opinions based upon study and experience and controlled by judgment.

A. K.

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A TEXT-BOOK OF GYNECOLOGICAL DIAGNOSIS. By GEORG WINTER, M.D., Professor and Director of the Gynecological Clinic in the University of Berlin, with the collaboration of CARL RUGE, M.D., of Berlin. Edited by JOHN G. CLARK, M.D., Professor of Gynecology in the University of Pennsylvania. Translated from the third revised German edition by R. MAX GOEPP, M.D., Pp. 670; 350 illustrations. Philadelphia and London: J. B. Lippincott Company, 1909.

It seldom falls to the lot of the reviewer to read a volume with greater pleasure than the present. Those who know its earlier German editions will not be surprised at the technical excellence of the translation, and for them any detailed review is superfluous. The volume opens with a section upon the general diagnosis of gynecological cases, which is complete in detail. Besides the usual methods of examination there are sections devoted to cystoscopy, bacteriological diagnosis, and microscopic examination, the latter by Ruge. The second and by far the largest portion of the work is concerned with special diagnosis. Under this heading is included the study of diagnostic methods as applied to all known gynecological conditions. Beginning with the findings in the normal pelvis,

anatomical, palpatory, and histological, the author proceeds to a satisfactory study of the diagnosis of normal pregnancy and of the disturbances which may arise during gestation. Ruge again contributes a most excellence section upon the microscopic diagnosis of pregnancy and of expelled membranes. Space forbids any detailed description of the excellence of this portion of the work; enthusiastic approbation would be our criticism. Displacements of the uterus and the diagnosis of myomas fill up the next eighty pages. To the general reader these chapters will be most instructive, and will certainly be appreciated. The diagnosis of ovarian tumors is followed by the diagnosis of malignant disease of the uterus. As is to be expected, great emphasis is laid upon the early recognition of uterine carcinoma, and the microscopic examination is insisted upon as an aid to this end. A remark made by the author in considering this matter is so timely as to merit incorporation here. In insisting upon the greater need for the microscopic study of suspicious tissue by the general practitioner as compared to the specialist, he remarks that the latter, by his constant training, is often able to differentiate by palpation and specular examination between benignancy or malignancy, while the former "ought, if he were in the habit of making accurate examinations, to see a great many doubtful speculum pictures and feel a suspicious hardness in a great many cases; and for this reason he ought to resort more to the microscope in the diagnosis of cervical cancer than the expert specialist." It is sad to think of the numberless lives now being denied the only chance because men of limited experience will persist in waiting for indubitable macroscopic signs instead of referring the case for operation upon the strength of microscopic study. Sarcoma of the uterus, neoplasm of the vagina and vulva, and microscopic diagnosis of malignant diseases of the uterus, vagina, and vulva follow, the last mentioned by Ruge. The diagnosis of tubal disease, of pelvic peritonitis, and of parametritis is next considered. The last two mentioned sections will particularly repay careful reading. The differential diagnosis of uterine catarrh is too generally neglected by specialists as well as general practitioners. We can heartily commend the two dozen pages upon this subject, and in particular would call attention to the three pages upon gonorrhœa with which the section closes. The division is here made into positive, probable, and uncertain signs. In the second class he has placed pyosalpinx, stating that "it has never been definitely proved that this may be due to some other infection, as tuberculosis." While many will not agree with him in this sweeping statement it has great significance when coming from such an authority. Ruge contributes a section of a dozen or more pages upon the diagnosis by the microscope of endometritis, both of the cervix and body. This portion of the book closes with the diagnosis of diseases of the urinary apparatus—the urethra, bladder, ureter,

and kidney being considered. The third and last division of the work, comprising over fifty pages, is devoted to analytical diagnosis; the causes of hemorrhage, amenorrhœa, dysmenorrhœa, sterility, and the analytical diagnosis of abdominal tumors being the subjects dealt with. We look upon this portion of the work as exceedingly valuable, since, summing up as it does much that is scattered through the body of the book, it will be the means of finally fixing in the mind of the reader many diagnostic viewpoints of great importance. A review of this work would be most incomplete were the translator's work to pass unnoticed. Dr. Goepf has faithfully performed a most arduous task, and has produced a translation which, while departing in no respect from the literalness demanded, has an enviable smoothness in construction.

We are confident that the profession in this country and England will give the volume a very hearty welcome. W. R. N.

PRATIQUE DE LA CHIRURGIE ANTISEPTIQUE. Leçons Professées à l'Hôtel Dieu. By le Docteur JUST LUCAS-CHAMPIONNIÈRE, Honorary Surgeon to the Hôtel Dieu, Member of the Academy of Medicine, Member of the Council of Hygiene and Health of the Department of the Seine. With a portrait of Lord Lister. Pp. 464. Paris: G. Steinheil, 1909.

IN 1874 Lucas-Championnière made, at the Hospital Lariboisière, the first trial in France of antiseptic surgery, which he had seen employed by Lister at Glasgow in 1868; in 1876 he published his *Manuel de Chirurgie Antiseptique*, and this was the first adequate presentation of the subject in any language. The present volume, comprising 33 chapters, is an entirely new work, founded on the veteran surgeon's lectures at the Hôtel Dieu, and addressed especially to young surgeons or to those practitioners whose intellects are not beclouded by the teaching of certain masters, or enslaved by "écoles théoriques et intransigeantes."

The work, in fact, is as much a polemic against aseptic surgery as it is an exposition of antiseptic practice. The author does not hesitate to mention by name the lamented Terrier, to whom more than to any other one man is due the revolution in the administration of hospitals in France, who for so long stood at the head of French surgery, and without whose devoted attention to the development of aseptic technique the surgery of the viscera could never have reached its present advanced state; and Quénu, one of Terrier's most distinguished pupils, is also named; and the modern operating room, its furniture, the aseptic costume of the surgeon, and every modern improvement, are unmercifully ridiculed and derided as

unnecessary and, therefore, undesirable. This raucous voice from the past laments the disappearance of the carbolic spray, which he abandoned because his assistants took malicious pleasure in neglecting its use in his absence, that is to say, at times when it would have been most useful; and he thought it better to abandon it than to make bad use of it. He no longer uses the green protective only because it is no longer manufactured. He has compromised for giving up the impermeable dressing by the employment of copious coverings of weak iodoform gauze. He places his main reliance on carbolic acid; soaks his hands and instruments in it; swabs out all his wounds with it; drains all his cases of operation for the radical cure of hernia with a rubber tube "because it makes the scar firmer;" wears no gloves; prohibits the use of nail brushes on the skin of surgeon or patient; and glories in the fact that in the filthiest surroundings he is able to secure clean wounds by these means.

No surgeon worthy the name will ever fail to appreciate the debt of modern surgery to antiseptics; and it would be well if many modern surgeons would stop seriously to consider the many slight, but in the aggregate important, lapses from the antiseptic method which they constantly permit themselves. Says Championnière: "The perfection of modern surgery is such that we have not the right to deprive those who intrust themselves to us of the least of the advantages which we can give. An apparently slight neglect is enough to lead to useless suffering, and you will often see it. You will see a little suppuration in one corner of the wound. You will see crusts which last indefinitely; you will see a wound which has gaped open at the site of one suture; you will see, what is graver yet, a suture discharged from the wound some days, weeks, or months after the operation. Now, *in the immense majority of cases*, these little incidents, which inflict useless miseries on the patient, are faults or negligences of the operator."

The further one reads into the volume, the deeper becomes the impression that it speaks the truth, and nothing but the truth, but not always the whole truth. Because a thing is possible, it is by no means always expedient; and to ignore the advantages wrought by asepsis is characteristic of "intransigence" of a marked degree. Yet the author's results by his strict adherence to antiseptic methods are marvellous; he cites, for instance, his series of excisions of the knee, with only one death (*delirium tremens*), in the 133d case; he claims to have operated on more fractures of the patella than any surgeon in the world, and with none of the precautions adopted in aseptic surgery, and with never a case of septicæmia; he mentions his 1135 operations for the radical cure of hernia, with only 4 deaths, none from septicæmia; he was the first to practise cerebral surgery, and he remains, he asserts, one of those who have practised it longest and most completely, but with never a single case of sepsis in his experience. He does not blow his own horn so loudly in regard to abdomi-

nal surgery; and he claims that aseptic surgery, which finds its particular field here, succeeds because the peritoneum is less disposed than the other tissues to infection through the air. The failure of aseptic methods in other departments of surgery he holds an insuperable objection to its general adoption. Granted that these premises are correct, which we do not believe, it is surely enough to be thankful for that modern abdominal surgery has developed from the practice of aseptic methods; and even though aseptic practice has its limitations, it is an advance in suitable cases, and in such must not be lightly abandoned.

A. P. C. A.

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THE PRINCIPLES OF BACTERIOLOGY. By A. C. ABBOTT, M.D., Professor of Hygiene and Bacteriology in the University of Pennsylvania. Eighth edition; pp. 631; 100 illustrations. Philadelphia and New York: Lea & Febiger, 1909.

EIGHT editions tell the story of Abbott's *Bacteriology*. Originally published when bacteriology may be said to have been in its mewling and puking infancy, it has been since its birth perhaps the most popular students' book and has exerted a marked influence in diffusing a knowledge of bacteriology; indeed, one may say that much that most practitioners of medicine, as well as avowed bacteriologists, know of the subject is founded upon what they learned originally from Dr. Abbott's book. Extended comment of the new edition is scarcely necessary. It has been brought thoroughly abreast of the times, and now contains the important facts and the latest trustworthy opinions regarding a branch of medicine that is advancing with rapid strides. Special attention has been paid to infection and immunity, including the antitoxic, bactericidal, and phagocytic properties of the blood, and the use of vaccines in the prevention of certain infections, etc. As heretofore, the book may be warmly recommended; there is no better of its size.

A. K.

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VORLESUNGEN UEBER TUBERKULOSE: I. DIE MECHANISCHE UND PSYCHISCHE BEHANDLUNG DER TUBERKULOSEN BESONDERS IN HEILSTATTEN. By DR. GEORGE LIEBE, Director of the Heilanstalt Woldhof Eigershausen. Pp. 275. München: J. F. Lehmanns, 1909.

THE vast amount of literature on tuberculosis that has appeared during the last few years is so appalling that only the stoutest-hearted dares even contemplate keeping up with a fraction of what

has been written. It is not strange that much of the literature on the sanatorium treatment of tuberculosis should come from Germany, for there the sanatorium treatment has been applied far more extensively than in any other country. Dr. Liebe has prepared his lectures on tuberculosis so that they can be understood by students of medicine who wish to know about the sanatorium treatment without a sojourn in one of these institutions. The first part of his book deals with the mechanical and physical treatment in sanatoriums and contains much that is admirable. He is inclined to allow his patients much more latitude in regard to exercise than many sanatorium physicians approve of, and for this he is censured by Schroeder. He believes in pulmonary gymnastics and also in teaching patients how to breathe properly. His attitude on alcohol is similar to that held by many physicians in America—that it should be dispensed only by the druggist and not as wine or beer. He deals with many subjects that are not ordinarily touched upon, such as religion and the church, the ethics of the sanatorium, as well as the desire for learning that many of the patients manifest. American literature is not particularly well covered, though the German literature is very well gone over, and sixty pages are devoted to notes and criticisms of various articles from the literature. On the whole, the book contains much that is of interest, little, however, that is new; but the author's opinions and criticisms of the various subjects that he discusses makes the book interesting reading.

L. B.

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PHYSICAL DIAGNOSIS. By RICHARD C. CABOT, M.D., Assistant Professor of Medicine in the Harvard Medical School, Boston. Fourth edition; pp. 579; 245 illustrations. New York: William Wood & Co., 1909.

SINCE Dr. Cabot's *Physical Diagnosis* has long since achieved a permanent place in medical literature and is widely used in medical colleges as the required text-book, one need do no more than chronicle the issuance of a new edition. The book has been materially improved and considerably enlarged; many minor changes and alterations have been made throughout; the chief additions concern the use of the free ear in auscultation, the discussion of bronchiectasis, and the differences between the sides of the chest. The author states also that some of the pictures have been changed, and he hopes improved; but in this instance, realization falls short of hope: most of the illustrations remain as they have always been, very poor examples of the engraver's and printer's art—the only bad features of an excellent book.

A. K.

THE THERAPEUTICS OF RADIANT LIGHT AND HEAT AND CONVECTIVE HEAT. BY WILLIAM BENHAM SNOW, M.D., Editor of the *Journal of Advanced Therapeutics* and late Instructor in Electrotherapeutics in the New York Postgraduate School. Pp. 119; 15 illustrations and 8 plates. New York: Scientific Authors' Publishing Co., 1909.

THE author modestly proclaims in his preface that he has been induced to write this condensed manual at the request of students and other members of the profession, and not at all because of the fact that he wanted to inflict the medical public with his own views. He further states that in considering the subject, attention will be devoted to the elucidation of physiological actions, practical indications, and methods of employing radiant light and heat from the modern point of view, by which, of course, he means his own point of view.

This is a beautiful book. It is full of illustrations of the different forms of electrical implements, the number and variety of which is beyond one's imagination, interspersed here and there with a new cabinet by the author, with modifications and methods of treatment. The explanation of the physiological effects of light and heat is well set forth, providing one is willing to believe what the author has to say. For instance, when discussing the derivative effects produced by extensive exposure he states that "there is pronounced lessening of the quantity of blood in the congested regions and large arteries and veins, lowering of arterial tension, relief of the overworked heart, and coincidentally promotion of extensive elimination of the locked-up products of poor metabolism." Most of the book is taken up with the methods of application of radiant light and heat and the benefits to be derived therefrom. According to the author, there is no disease to which the human is heir which cannot be benefited by electricity. All sorts of pains are relieved, postoperative cases benefited, myalgias cured, and the different germs which cause inflammation brought into a state of complete inhibition. The Röntgen rays, according to him, can cure cystitis, prevent and cure otitis media, whether acute or chronic, carbuncles, furuncles, felon, suppurative tonsillitis, tuberculous arthritis, adenitis, pelvic congestions, ozena, postoperative iritis, etc. Radiant light and heat, according to him, can cure varicose ulcers, lupus and allied conditions, eczema, psoriasis, all sorts of spinal conditions and nephritis, to say nothing of arteriosclerosis. This reads like an advertisement, and expresses about as well as anything could what the book is.

T. H. W.

# PROGRESS OF MEDICAL SCIENCE.

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## MEDICINE.

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UNDER THE CHARGE OF

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**A New Sputum Test.**—FALK and TEDESCO (*Wien. klin. Woch.*, 1909, xxii, 954) have proposed a method for differentiating disease processes limited to the bronchial mucosa from those which have extended to the lungs. Their method is based on the fact that salicylic acid, present in the blood, appears in inflammatory exudates, but is not excreted by the bronchial mucosa. Patients with expectoration are given 2 grams of sodium salicylate. The sputum is collected for the next twelve to fifteen hours and examined as to its content of the drug in the following manner: The entire sputum, slightly acidified, is thoroughly shaken with five times its volume of 96 per cent. alcohol. Albumin and mucous-forming bodies are precipitated in coarse flocculi and removed by filtration, since they contain none of the salicylate. The clear filtrate is rendered slightly alkaline and evaporated on a water bath; the residue is dissolved in water, slightly acidulated, and sugar of lead added. The precipitate is removed by filtration, the precipitate being washed, and the acid filtrate is extracted with ether. The ethereal extract is now evaporated, the residue taken up in 10 c.c. of water, and 1 c.c. of 10 per cent. aqueous ferric chloride is added. In the presence of salicylates, the solution is colored violet. Patients suffering with acute catarrhal bronchitis, chronic bronchitis of emphysema, bronchial asthma, purulent bronchitis, bronchiectasis, and bronchial catarrh of cardiac origin, all reacted negatively. In two cases of lobar pneumonia a strong positive reaction was seen; in one diplococci, in the other streptococci, were found in the sputum, with typical signs in the lungs. The reaction gradually lessened until the crisis, then quickly disappeared. The intensity of the reaction was roughly proportional to the extent



of the lesion. In two other cases without physical signs in the lungs, proved by autopsy to be central pneumonia and bilateral gangrenous pneumonia respectively, a marked reaction occurred. In tuberculosis the results varied considerably. A positive reaction was met with in all cases, but the intensity of the reaction was not proportional to the clinical severity or extent of the pulmonary process. In general, however, the acute cases gave a stronger positive reaction than the chronic ones. From their experience with the test, Falk and Tedesco conclude that a repeatedly negative test is strong evidence that the disease process is limited to the bronchial mucosa. A very strong reaction (dark violet color, even after diluting five to ten times) indicates an extensive inflammatory (exudative) process in the lung itself, as in pneumonia. In doubtful cases in which the diagnosis lies between bronchitis and tuberculosis, a positive reaction favors the latter. Furthermore, cases of central pneumonia, unrecognizable by physical signs, should be strongly suspected with a marked positive reaction.

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**The Relationship of Anæmia Pseudoleukæmica Infantum to Rachitis.**—ASCHENHEIM and BENJAMIN (*Deut. Archiv f. klin. Med.*, 1909, xevii, 529) have made a careful clinical and pathological study of 5 cases of so-called anæmia pseudoleukæmica infantum, and in addition have analyzed 70 recent cases in the literature. In all but 5 of these cases rickets existed definitely, and in 50 per cent. of them it was of severe grade. In the majority of cases in which autopsy has been performed, lymphoid "degeneration" and erythroblastosis of the bone marrow have been demonstrated. Similar alteration of the marrow is not uncommon in rickets. Aschenheim and Benjamin believe that anæmia pseudoleukæmica infantum results from the degenerative process of the bone marrow, which is one of the effects of rickets. The disease is, therefore, not a clinical entity, but rather a sequel of rachitis, comparable to tabes dorsalis after syphilis. As an expression of the lymphoid marrow, they find a marked reduction of the polymorphonuclear neutrophils, and the numerous nucleated reds are due to red cell hyperplasia. The blood picture need not include a diminution in number of the erythrocytes or a leukocytosis, as their own cases and others in the literature show. The large mononuclears are usually increased. Myeloid metaplasia of the spleen is frequent, and even the liver may take part in the blood formation. The authors suggest that the condition be designated rachitic splenomegaly, and that the old names, anæmia splenica, anæmia pseudoleukæmica infantum, and anæmia pseudoperniciosa, be dropped.

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**A Peptid-splitting Ferment in Cancer of the Stomach.**—Fischer has shown that digestion progresses further with proteins in carcinomatous stomach contents than in the normal stomach. Thus, the HCl deficit with normal chlorine content is explained. By the splitting of the proteins into polypeptids and eventually into mono-acids and diamono-acids, amino groups become free; these bind HCl, and, therefore, when present in sufficient quantity, may produce an HCl deficit, while the total acidity increases through the presence of the free carboxyl groups. This extended hydrolysis of proteins cannot be carried on by the pepsin-HCl of the gastric juice, but is done normally in the intestines by trypsin

The blood also contains ferments capable of similar work. In the absence of pancreatic juice and blood in the carcinomatous stomach contents, it would appear that another ferment must be present, which is capable of extended hydrolysis of proteins.

NEUBAUER and FISCHER (*Deut. Archiv f. klin. Med.*, 1909, xevii, 499) have studied the gastric contents in health and disease, with a view of determining the presence of a specific ferment in carcinoma. They selected a polypeptid, glycyltryptophan, with which they test for the presence of a peptid-splitting ferment; if present, tryptophan is formed. This may be recognized by a reddish-violet coloration on the addition of bromine water. Numerous experiments have shown that there is present in malignant tumors, both sarcomas and carcinomas, a ferment capable of splitting glycyltryptophan very much more rapidly than that found in normal tissues and benign tumors. No cleavage whatever is produced by the pepsin-HCl from human and canine stomachs. Experiments have also shown that possible peptid-splitting ferments in yeasts, moulds, and bacteria are eliminated, with the technique adopted, by filtration of the gastric contents or, more simply, by the addition of toluol. Gastric contents which contain pancreatic juice or blood are obviously unsuited for examination. The absence of the former may be determined by testing for bile with dilute tincture of iodine, while the latter is tested for by the acetic acid-ether and guaiac tincture test of Weber.

*Technique.*—The test breakfast is removed after one-half to three-quarters of an hour. It is tested for bile (and consequently pancreatic juice) and for blood; if either are present, the specimen must be discarded and another obtained. The gastric contents are then tested with bromine water to exclude the presence of tryptophan; if this test is positive, it also necessitates obtaining a fresh specimen. All of the three tests being negative, about 10 c.c. of filtered gastric contents is placed in a test-tube with a little glycyltryptophan, covered with toluol to prevent bacterial growth, and put in the incubator for four hours. With a pipette 2 to 3 c.c. is withdrawn and acidified with a few drops of 3 per cent. acetic acid. Bromine vapor is allowed to settle in the test-tube until a light brownish color is seen in the upper part of the tube; the contents are shaken, and if a rose color develops, free tryptophan is present, and the test is positive. An excess of bromine must be avoided, as it causes a disappearance of the rose color. If no rose color is seen, one adds bromine fumes carefully as before, shakes, and observes. One continues in this way till the fluid in the test-tube shows a light yellow color, which indicates an excess of bromine and a negative result. Calcium chlorate,  $\frac{1}{16}$  saturated aqueous solution, may be substituted for the bromine; the same color and similar difficulties are met with.

Applying their method to clinical work, Neubauer and Fischer obtained negative results in 4 normal stomachs, 10 ulcers of the stomach, 12 gastric diseases other than carcinoma, 4 cases of suspected carcinoma, and in the vomitus of 2 cancer cases. A positive result was obtained in 17 cases of cancer of the stomach and in 6 suspected cases. The results demonstrate the presence of a ferment (which is inactivated by 0.36 per cent. HCl) in carcinoma of the stomach, which hydrolyzes polypeptids, and indicate its usefulness as a diagnostic procedure.

**The Effect of Febrile Diseases in Diabetes Mellitus.**—BRASCH (*Deut. Archiv f. klin. Med.*, 1909, xcvi, 508) has studied the effect of intercurrent febrile diseases on the metabolism of diabetics and arrives at the following general conclusions: (1) Febrile diseases may increase or decrease the glycosuria in diabetes mellitus. (2) Mild cases of the disease usually show a decrease in the quantity of glucose, without subsequent ill effects. (3) Increase of glycosuria and the occurrence of acetonuria may be seen in severe cases of diabetes during febrile diseases; in some instances, however, no change in the excretion of sugar is noted during the course of the fever, but subsequently the patients rapidly decline. (4) The cause of the fever is of less moment than the severity of the diabetes.

**Experimental Functional Mitral Insufficiency.**—LIAN (*Archiv. des mal. du cœur, des vaisseaux, et du sang*, 1909, ii, 569) has studied experimentally in dogs the functional insufficiency of the auriculo-ventricular valves, which occurs shortly after the onset of asphyxia. The insufficiency dependent on asphyxia is the result of several factors; an increase of arterial pressure in both the greater and lesser circulations, the malnutrition of the heart from the poorly oxygenated blood, and the action of the pneumogastric nerve in slowing the heart rate, increasing the length of the diastole, and diminishing the tonicity of the myocardium. The tracings of the volume curve of the left auricle show that insufficiency begins synchronously with the onset of ventricular systoles. It disappears as soon as the animal is allowed to breathe normally, but may be brought on again by subsequent production of asphyxia. It was possible to cause insufficiency at intervals of several days in the same dog, there being in the meanwhile apparently complete recovery. In several instances functional insufficiency was produced without opening the thorax; it was accompanied by a well-marked systolic murmur localized at the apex. Neither stimulation of the pneumogastric, or sudden compression of the aorta usually cause insufficiency. The conditions which appear to be necessary to the production of functional insufficiency of the mitral valve are a diminution in the tonicity of the myocardium, and an overdistended left ventricle.

**Blood Regeneration from Diminished Oxygen Tension.**—KUHN and ALDENHOVEN (*Deut. med. Woch.*, 1909, xxxv, 1958) refer to the recent studies on regeneration of the blood, with increase in the total volume of the blood, following the use of the suction-mask (Saugmaske). The red count may be increased 1,000,000 to 3,000,000 cells per cubic millimeter by the daily use of the mask, and, indeed, the rise begins almost at once. There is a coincident, but slower, augmentation in hemoglobin. Exactly similar findings may be obtained in persons going from the sea level to high altitudes. Likewise, after dyspnoea, polycythemia and increase in hemoglobin have been noted, lasting for some time. As experiments have shown, these results are not due to a loss of plasma (concentration of the blood); there is an actual increase in the total quantity of blood and of hemoglobin, and the bone marrow in the shafts of the long bones is red, rather than fatty. The cause of these phenomena is a lowered oxygen tension in the tissues. The rapid regeneration which follows hemorrhage is probably due to the

same cause. The response is extremely prompt, as Müller has shown. It is well known that the administration of arsenic leads to increase of the erythrocytes. Similarly it has been noted that the administration of tuberculin is often followed by an increase in the red cells. It is equally well known that arsenic is a hemolytic poison. Kuhn and Aldenhoven, therefore, have attempted to explain these facts by experiment. They made a series of observations in guinea-pigs to which atoxyl and tuberculin were administered, and found an initial fall in the blood count, followed by a rise, due, they believed, to a primary lessening of the oxygen tension from destruction of red cells; this resulted in stimulation of the bone marrow sufficient to produce a subsequent rise. To determine this point the experiments were repeated on a second series of animals which were kept in cages so constructed that the inspired air could be surcharged with oxygen. In all the animals there was now a steady decline in the number of red cells in the blood. They conclude that arsenic does not affect the bone marrow primarily, but that the stimulus to erythropoiesis is due to the lowered oxygen tension caused by destruction of red cells.

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**The Auriculonodal Junction.**—In the study of the system of conduction fibers in the hearts of cats, rabbits, monkeys, dogs and goats, COHN (*Heart*, 1909, i, 167) has found that there is constantly present a connection between the fibers of the auriculoventricular node of Tawara and the muscle of the auricle. In the cat the fibers of the dorsal portion of the node become thicker and gradually pass into the auricular fibers. Sometimes two or three of the smaller fibers unite to form an auricular fiber. The number of nuclei in the muscle fibers decrease progressively in the passage from node to auricle, but the transverse striations, which are rarely seen in the nodal fibers, come out more clearly in the transition fibers, and become fully developed in the auricular fibers. In the monkey, at the point of passage from auricle to node the fibers become plumper, more nearly parallel, and the fibers of one become continuous with those of the other. The passage from auricle to node is so gradual that it is impossible to say where one begins and the other leaves off. In dogs, cats, and rabbits collections of ganglion cells were found close above the point of transition from auricle to node. In the monkey no nerves were found in or near the bundle or node, but many were seen in the interauricular system. The position of the A-v node was found to be variable. While it is usually found on the right side of the interauricular septum, it may be in the mid-line, or even nearer the left side. These variations are explained as due to embryological variations in the formation of the auriculoventricular groove at the membranous septum.

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**The Treatment of Amœbic Dysentery in the Canal Zone.**—From 1905 to 1909 there were 211 patients treated for amœbic dysentery in the Ancon Hospital. In 82 of these various methods of treatment were used, including opiates, ipecac, castor oil, magnesium sulphate by mouth, and local irrigations of quinine, thymol, silver nitrate, starch, boric acid, tannic acid, etc. In this series the mortality was 39 per cent., and the average time in the hospital twenty-eight days. Another series of 129 cases was treated by what OEEKS and SHAW (*Medical Record*,

1909, lxxvi, 806) call the "rest-supportive" method. The average time in the hospital for these cases was twenty-one days, and the mortality 18 per cent. The essential features of the treatment were absolute rest, a strict milk diet, saline or water irrigations, and bismuth subnitrate in heroic doses. A mild irrigating fluid is preferred since it cleanses the mucous membrane without irritating it and favoring the invasion of fresh areas. A milk diet provides the most perfect food, and causes less intestinal putrefaction than others. The bismuth is given in doses of 1 dram to 1.5 dram (by measurement) every three hours until there is a general improvement—from three to fifteen days. Toxic effects were never seen. There have been no relapses among the cases receiving this treatment. Herriek (*Ibid.*, p. 810) groups those cases of amoebic dysentery needing surgical treatment in three classes—those that have become chronic and remain so under the best medical treatment; acute fulminating cases with extreme toxicity; and severe acute cases resisting medical treatment, and going down hill. Most of the cases operated on at Ancon belong to the last group. As to the operation to be performed, he believes that in the earlier, milder cases, when the process is mainly on the surface layers of the bowel, appendicostomy with irrigation of the bowel is indicated. When, however, the deeper layers of the intestines are involved as in the more severe cases, complete rest of the large bowel is desired, and cecostomy is the operation of choice.

**Actinomycotic Cerebrospinal Meningitis.**—HENNY (*Jour. Path. and Bact.*, 1909, xiv, 164) reports the case of a man, aged twenty-six years, who developed an abscess of the right upper jaw after having had a carious tooth extracted. Incision of the abscess was followed by partial healing and sinus formation. On four occasions the abscess was opened. Ten days after the last operation—over one year after the onset of the trouble—he began to develop cerebral symptoms. Headache, pain over the spine, and fever were followed by rigidity of the neck, Kernig's sign and opisthotonos. Death occurred in the fourth week. On lumbar puncture about 2 c.c. of very thick fibrinous fluid were obtained. At autopsy the base of the skull and the spinal cord were covered with a thick, viscid exudate. Typical actinomycotic granules were obtained from the cerebrospinal exudate during life, and from the operation wounds. Anaërobic cultures yielded a growth such as is described as typical for the organism of actinomycosis. An examination of the literature reveals only twenty-five similar cases, and in several of these the identity of the etiological organism is extremely doubtful. In the great majority of the reported cases the involvement of the meninges was secondary to a general infection or to a primary growth elsewhere, and was the determining cause of death. The lungs and bronchial glands are the common seat of the primary lesion. In only three cases was the infection due to direct extension from the tissues of the neck and face.

## S U R G E R Y.

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UNDER THE CHARGE OF

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**Ureterocele (Hernia of the Ureter).**—CACCIA (*Archiv. gén. de chir.*, 909, iii, 991) collected 22 cases from the literature and reports two personal observations. It may or may not be accompanied by a peritoneal sac, that is, it may be paraperitoneal or extraperitoneal. Each variety may occur alone or be accompanied by a cystocele or hernia of the bladder. Any of these varieties may be found in the inguinal or femoral regions. Ureterocele is very rare, yet one should think of it if he finds an abnormal cord in contact with the hernial sac. The pre-operative diagnosis, although it has not yet been made, is possible. The clinical characteristics which permit it are as follows: There will be incomplete reducibility of a hernia, in connection with which there is felt a soft cord, which is not reducible, does not feel like an intestinal wall, a varicose vein, nor an empty hernial sac. Gurgling on reduction of the hernia is absent, and there may be perceived coincidently a hydro-nephrotic sac. Ureteral difficulties may be present, characterized by a diminution of the secretion of urine especially upon the application of a bandage, and their disappearance after the removal of the bandage. Evidence may be produced by the cystoscope and the ureteral catheter. There may be vague symptoms, such as painful micturition, hematuria, abdominal and lumbar pains from intermittent hydronephrosis. In the course of the operation the ureteral contractions should be watched for. The prolapsed portion of the ureter is usually dilated, and the weight of the urine, the vis à tergo, and the ureteral contractions, facilitate the course of the urine. Extraperitoneal ureterocele is probably congenital. Paraperitoneal ureterocele has a complex mechanism and its causes are multiple. Ureterocele combined with a cystocele has also a complex pathogenesis. If the portion of the ureter adjacent to the bladder is prolapsed, the cystocele is only a concomitant lesion, the ureterocele being simple and not due to the cystocele. The simple, paraperitoneal, femoral ureteroceles are more frequent than the inguinal, because as the experimental evidence shows, prolapse into the femoral canal is more easy than into the inguinal canal.

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**The Late Results of Removal of the Breast for Cancer.**—FIDELIN (*Archiv. gén. de chir.*, 1909, iii, 999) reports the results of a study of the late results of operation for cancer of the breast in 234 cases operated on by Maclaure, Guinard, Hue, Routier, and Schwartz; and of a detailed analysis of the work of Handley upon cancerous permeation. The

average duration of life in patients with cancer of the breast and not operated on, is forty-four months. While the surgical treatment is not ideal, at the present time it is our only means of arresting the progress of the growth, that is, the wide and early operation. Definite cure is rare; in fact, it can never be considered absolute, because one sees recurrences twenty and thirty years after operation, although in the interval no disturbing sign was manifest. The progress realized by surgery in the last half century, is encouraging. According to Depage, who studied a large number of statistics, it was found that the percentage of cures three years after operation, between 1865 and 1875, was 9.4 per cent.; between 1875 and 1885, 10 per cent.; between 1885 and 1895, 34.3 per cent.; and between 1895 and 1905, 46.3 per cent. The recurrences from 1865 to 1875 were, locally, 76 per cent.; glandular, 8.4 per cent.; and at a distance, 7.5 per cent.; from 1875 to 1885, locally, 72 per cent.; glandular, 6.2 per cent.; and at a distance, 10 per cent.; from 1885 to 1895, locally, 45.5 per cent.; glandular, 8.4 per cent.; and at a distance, 19 per cent.; and from 1895 to 1905, locally, 29 per cent.; glandular, none; and at a distance, 23 per cent. Surgeons are not agreed on the question of the detachment of the muscles. Some conserve the pectorals, arguing that muscular recurrences are rare, and that by sacrificing these muscles the patients are much crippled. Others remove them systematically, because in certain cases neoplastic nodules are found under the pectorals, which are apparently healthy. The statistics permit discussion on this point. Muscular recurrences have been observed in patients who have undergone a wide operation by the Halsted method. The progressive diminution of recurrences can be attributed only to the improved operative technique. Modern methods at first view appear to give a lessened period of survival, but this proves erroneous when applied to a large number of cases. When we find an ideal method of operation, the recurrences will take place only when there exist unrecognizable metastases at the moment of operation (Handley). According to Handley, a certain number of recurrences, which formerly were regarded as fatal, are due to the negligence or rather the false conception of the operator regarding the mode of dissemination of cancer. He says that in the future we can avoid these by resecting widely the superficial fascia, along which the infection extends to distant parts.

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**Experimental Artificial Anemia in Intracranial Operations.**—SAUERBRUCH (*Zentralb. f. Chir.*, 1909, xxxvi, 1601) had previously shown that with the aid of his pneumatic cabinet, through the local effect of sufficient excess of pressure on the opened skull, the venous hemorrhage from bone and brain could be completely arrested, while the arterial could be considerably diminished. The compression of the capillaries and veins required a pressure of from 20 to 30 mm. of mercury, while the compression of the arteries required a pressure of at least 70 mm. of mercury. At the same time the brain was more or less compressed and contracted. The method is not, however, available for man. The frequent occurrence of air emboli proved to be a great danger, and the technique of the method was too complicated to be of value for other than experimental purposes. More recently, Sauerbruch has been experimenting upon the hemostatic effect produced by the

reduction of the normal atmospheric pressure. The animal was placed in the pneumatic chamber, as for the performance of an intrathoracic operation, the head being outside, the breast, abdomen, and extremities inside the chamber. An air tight closure was made about the neck. The opening was then made in the skull which was outside, and as soon as the air pressure within the chamber was reduced to about 15 mm. of mercury, the venous hemorrhage was considerably diminished and at 20 mm. pressure it was completely arrested. The brain contained little blood, and consequently its surface was depressed, about 1 cm. In this period the large venous sinuses could be opened without hemorrhage. The arterial bleeding was reduced only when the air pressure within the cabinet was diminished to about 40 mm. Upon the removal of the lowered pressure within the cabinet, the brain soon increased to its normal size, and the bleeding returned. The decrease of pressure over the chest leads to a marked expansion of the chest, and to a marked aspiration of venous blood into the right heart. The breathing and heart action, however, are not seriously disturbed. The capillaries in that portion of the body within the cabinet, especially in the abdomen, are considerably dilated, and the dilated vessels take up a large part of the circulating blood. A laparotomy undertaken at the same time as the opening of the skull will demonstrate the filling of the veins of the abdomen. The blood pressure in the carotid and femoral arteries is not changed, that in the jugular vein is decreased during diminution of pressure in the cabinet. Pressure on the abdomen increases the pressure in the abdominal vessels and induces a normal filling of the brain with blood. After a ligation of the external jugular on both sides, the intracranial venous anemia, from decreased pressure within the pneumatic cabinet, either is not obtained or is obtained only with difficulty. Nor does it occur if the abdomen is distended abnormally, as by an overfilled bladder or pregnant uterus. In dead animals the veins will be emptied by a pressure of 7 mm. of mercury within the cabinet, but pressure upon the abdomen immediately refills them. Air emboli do not develop with this method, because of the resulting diminution of the caliber of the vessels. Dangerous results from the effect of this method on the brain have not been observed.

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**The Diagnosis of the Dilated Renal Pelvis by Means of Filling it with a Colloid Silver Solution and Skiagraphy.**—VOELCKER (*Archiv f. klin. Chir.*, 1909, xc, 558) has employed this method in a series of cases, and has found it of value for the diagnosis of the position of the kidney, of the degree of dilatation of the pelvis, and of the degree of dilatation and position of the ureter. The normal pelvis reaches its maximum capacity at 2, 3, or 4 cm. The ureteral catheter is introduced to the renal pelvis, that is, to a distance of from 20 to 25 cm. Distention of the normal pelvis with the collargol solution usually gives rise to pain lasting about twelve hours, but to no permanent injury. Chronically dilated pelves give no pain when distended by the fluid. The ureteral catheter impregnated with bismuth is often left in position in the ureter. When the catheter is introduced to the kidney, the capacity of the pelvis may be determined as well as the existence of residual urine in it. The collargol is usually in a 2 per cent. solution, is a good antiseptic, and has a therapeutic effect upon the conditions due to the dilatation and



retention, sometimes very marked. It is only very slightly irritating, and, therefore, causes very little or no pain. That which does develop is due to the tension from the overfilling of the pelvis. As it is a dark fluid, it can be seen escaping into the bladder alongside the catheter. It also lends itself to the skiagraphy of the pelvis and ureter. The occurrence of pain in the kidney region and the escape of the collargol solution into the bladder will indicate that the pelvis is filled to its maximum. By this method Voelcker found that some pelves received 5 cm., others 10, 15, 30, 35, 120, and 150 cm. of the solution. The skiagrams were taken sometimes in the lying position and when possible during arrest of respiration. He has devised a special apparatus, which permits the skiagram to be taken in the standing position. While the normal renal pelvis is on a level with the first lumbar vertebra, in movable kidneys it varies, in some being on a level with the second, in some with the third, and in one case with the fourth lumbar vertebra. The ureter participated in the depression in three different degrees: (a) It sank entirely with the kidney, having a tortuous course without actual kinking; (b) it remained fixed throughout, kinking at its junction with the pelvis; (c) it remained fixed in its chief part, while its renal portion moved with the kidney. In these cases, and they proved the most frequent, the ureter was kinked, generally, a few centimeters below the renal pelvis.

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**Concerning the Question of Trephining in Traumatic Injuries of the Vault of the Skull.**—KUSNETZOW (*Archiv f. klin. Chir.*, 1909, xc, 1025) says that in compound depressed fracture of the skull operative intervention as soon as possible is the best method of treatment. One can say with certainty that the more frequent and the earlier the operation, the better the results. In simple fracture, operation is indicated if brain symptoms are present. Excessive delay may have an injurious effect upon the patient, so that the latter should be watched and operation done on the appearance of brain symptoms. Fissured fractures may be treated expectantly, but since even in mild cases of this variety dangerous symptoms may arise suddenly, the patients should be watched carefully. These dangerous symptoms may develop in the form of high temperature, convulsions, paralysis, and focal brain symptoms, and indicate urgent operation. The indications for operation in injuries to the skull should be decided after a careful study of every individual case and a consideration of all the clinical symptoms, avoiding dependence on the typical picture. In compound fractures resection of the skull, by means of the various chisels and bone forceps, is to be preferred to the typical trephining by means of the various trephines and drills. The chief requirements for the success of the operation are: (a) A sufficient widening of the defect in the skull; (b) a careful removal of the bone fragments and shreds of membrane, as well as a careful suturing of the deficient fibrous structures and torn brain substance; (c) careful hemostasis; and (d) the introduction of absorbent drains. Primary trephining in recent cases gives better results than the secondary, and shortens especially the period of wound healing. When meningitis complicates a compound fracture of the skull, the best method of treatment consists in a free exposure of the brain by a wide removal of a portion of the skull and the introduction of drainage

tampons under the opened dura mater. Extensive fractures of the skull, which have necessitated operative intervention, require long-continued observation of the patient afterward, in order to study the later condition of the central nervous system. Wounds of the frontal lobes may be accompanied by a peculiar change in the character and disposition of the patient, which has been described by Jastrowitz as a quibbling disposition.

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**Experimental Investigation Concerning the Increased Secretion of the Intestine in Dogs, in the Presence of Obstruction of the Bowel.**—BOESE and HEYROVSKY (*Deut. Zeit. f. Chir.*, 1909, cii, 183) says that recent works on ileus have made it probable that the majority of deaths from ileus are due to intoxication. There has been found in the fluid contents of the intestine a toxic substance which was capable of killing in a short time the animals experimented on. In the formation of these substances the bacteria play the chief role, and the increase of bacteria goes hand in hand with the liquefaction of the intestinal contents. Boese and Heyrovsky carried out experiments on dogs, the chief object of which was to determine the causes of the liquefaction of the hard fecal masses in the large intestine. After tying off the lower part of the large intestine in dogs, the hard, dry fecal masses were changed into a pulpy mass. This change was due to an increased secretion of the mucous membrane, beginning at the site of the ligature. The fluid contents of the lower, large intestine after the placing of the ligature, developed in the large intestine itself, and was not, as Talma has stated, the result of the accumulation in the large intestine of the secretion of the stomach and small intestine. The mucus secreted by the ligated portion of the large intestine is a poor culture medium for intestinal bacteria. Soon after the appearance of the transudate in the lumen of the bowel the bacteria grow rapidly, and through their influence the fecal masses are softened. The damage to the bloodvessels of the mucosa and submucosa of the intestinal wall, giving rise to the transudate in the lumen of the intestine, is to be traced to the influence of the stagnating intestinal contents. The formed feces are liquefied directly through the rapidly increasing bacteria, that is, through the gas formation which they cause. Atropine does not influence materially the secretion of the glands of the large intestine nor the liquefaction of the bowel contents in intestinal obstruction.

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**Statistics on Sarcoma of the Extremities.**—PIPERATA (*Deut. Zeit. f. Chir.*, 1909, cii, 195) says that he could not find in the literature large collections of cases of sarcoma of the extremities. The largest was that of Gross (165 cases) reported in 1879. Piperata reported 142 cases from Hochenegg's surgical clinic in Vienna, admitted between 1894 and 1907. Of these, 46 involved the soft parts, 21 the skin, 19 the fascia, 5 the muscles, and 2 the nerves. Of the bones, the femur was involved most frequently (30), then the tibia (13), pelvis (13), scapula (7), fibula (6), bones of the hand (5), clavicle (3), radius (1), and ulna (1). In 4 cases the fascia and bones were involved together, and in 5 cases the origin was not established. According to the statistics of Nasse also, the femur was most frequently involved. According to those of Reinhardt, the femur and tibia were involved with equal

frequency. Of the sarcomas of the long hollow bones in Piperata's statistics, 18 were periosteal and 13 myelogenous. The origin of 29 was not determined. Nasse found 19 myelogenous and 21 periosteal, while Reinhardt found 30 myelogenous and 15 periosteal. Sarcomas of the extremities occur at all ages, most frequently between fifteen and thirty-five years, more rarely in the very old and in children. Males were attacked much more frequently than females, and this agreed with the findings of Reinhardt. Of 83 of Piperata's cases occurring in men, 42 involved the long bones; and of 58 cases in women, 19 were in the long bones. As for the age, there was no essential difference between men and women. Concerning the etiology, it was worthy of notice that 38 patients traced the origin of the growth to a trauma. More than half of these cases were sarcomas of the long bones. There was no evidence of an hereditary influence in any of the cases, although two cases occurred in sisters. The duration of the disease preceding operation varied much. About half of the cases had existed between five months and one year, 25 were in the first three months, 30 were between one and five years, and 3 were said to have existed for over five years. The operation performed in most of the cases was radical, that is, a high amputation in the diseased bone or an exarticulation in the joint above. After this operation recurrence at the site of operation occurred in only one case. Resection of the involved bone was followed by a permanent cure in one case. In another the same operation was followed by local recurrence, requiring an enucleation twenty months after the first operation. Extirpation of the tumor from long bones was without success, except in one case, in which a second extirpation was followed by healing. Three cases were later saved by amputation, and in 3 cases the outcome was not learned. Of the 142 cases, 26 are known to be alive, and 88 are known to be dead. The result in the remaining 28 is not known. Of the 26 living patients, in 1 recurrence is said to have taken place; in 10 the period since the discharge from the hospital, not yet four years, is too short to permit definite judgment concerning the success of the operation. A permanent cure has taken place in 15 cases. Two cases have remained well for fourteen years, 6 cases for thirteen years, 2 for twelve years, 1 for eleven years, and 4 for four years.

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## THERAPEUTICS.

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UNDER THE CHARGE OF

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**The Treatment of Gastric Ulcer.**—VON LEUBE (*Deut. med. Woch.*, 1909, xii, 961) describes his routine treatment of gastric ulcer: (1) Absolute rest in bed for from one to two weeks. This relieves the pain and promotes the healing of the ulcer. After the tenth day the

patient should lie down two hours after dinner. (2) One glass of tepid Carlsbad water twice a day. (3) The application of hot stupes to the epigastrum, renewed every fifteen minutes during the daytime. At night a wet linen cloth is substituted. (4) A light diet of high nutritive value and easy digestibility.

In the severe hemorrhagic cases von Leube puts the patients to bed, gives one dose of 30 drops of a 1 to 1000 solution of adrenalin and an injection of morphine to quiet peristalsis, and complete abstinence of food by the mouth. He substitutes an ice-bag for the hot stupes and gives bismuth. When the stool shows no longer the presence of blood and there are no other signs of hemorrhage he cautiously commences a liquid diet. He replies to Lenhartz that while eggs and milk may bind the acid, at the same time they cause the secretion of more acid and increase the peristaltic movements of the stomach. He does not give iron because he says ulcer patients do not tolerate it well. Von Leube adds that a study of 25 cases on the liquid diet for two weeks did not show any marked reduction in the hemoglobin. He warns against the use of laxatives. By this routine method he has reduced the mortality from 13 per cent. in his first published series of cases to 0.5 per cent. in the present series. He reports in all 627 cases treated by this method. In 547 non-hemorrhagic cases 90 per cent. were cured, with no deaths. Most of these cures were effected in from four to five weeks. In the remaining 80 cases 90 per cent. were cured and there was 2.5 per cent. mortality. In his entire series 90 per cent. were cured, 8.5 per cent. improved, and in only 1 per cent. was there failure to improve. Von Leube says that while the Lenhartz diet may be given without much danger, yet he believes that a more restricted diet is safer. He also emphasizes the necessity of a complete abstinence from food during and immediately following a hemorrhage. In addition he states that while his patients may lose in weight at first, they have more than made it up by the end of the second week.

**The Present Status of the Serum Therapy of Epidemic Cerebrospinal Meningitis.**—FLEXNER (*Jour. Amer. Med. Assoc.*, 1909, liii, 1443) gives a brief statement of the status of the serum treatment of epidemic meningitis. The serum has now been extensively used in Great Britain, France, Germany, the United States, and Canada. Lately there has been a severe epidemic in France, and the serum has been employed in the treatment. The mortality in the cases will probably be less than 25 per cent. Flexner says that the serum treatment has been subjected to tests under a variety of conditions, some of which were as severe as probably ever occur, but yet he still advises caution in concluding that the case has been proved for the serum. He gives the results in 712 cases of epidemic meningitis treated with the serum, by different observers. Of the 712 cases, 224 died, a mortality of 31.4 per cent. The highest mortality occurred in the first two years of life and equaled 42.3 per cent. The second age period is from two to five years, in which the mortality was 26.7 per cent. The third age period embraces children from five to ten years of age, and gave the lowest mortality of all, namely, 15.9 per cent. The next period extends from ten to fifteen years, and gave a mortality of 27.7 per cent. The next period, of from fifteen to twenty years, showed a considerable rise

in mortality, equaling 32.7 per cent., and the last period, embracing the cases of twenty years and over, gave a mortality of 39.4 per cent. Flexner calls attention to the importance of early injections of the serum. Of those cases in his series injected during the first three days of the disease, the mortality was 25.3 per cent. Those injected from the fourth to the seventh day showed a mortality of 27.8 per cent., while those injected later than the seventh day gave a mortality of 42.1 per cent.

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**Intravenous Injections of Antidiphtheritic Serum.**—SCHREIBER (*Munch. med. Woch.*, 1909, xxxi, 1597) was induced to try intravenous injections of diphtheria antitoxin in serious cases of diphtheria by the results of the experiments of Berghaus. He has thus treated 20 cases of diphtheria, with only 1 death. This fatality occurred on the thirteenth day of cardiac paralysis. The child aged ten years received a subcutaneous injection of 2000 units and on the following day was much worse. Schreiber then injected intravenously 4000 units of antitoxin, which caused some improvement, but on the eighth day the heart became involved, and five days later the patient died. He is in favor of giving single high doses, 6000 to 10,000 units, rather than to repeat the dose in order to avoid a possible anaphylaxis. He thinks that high doses by infusion lower the temperature more rapidly than the subcutaneous injections. At the same time the general condition improves more rapidly. However, he believes that the intravenous injections do not have as good an effect on the local process. Schreiber says that if an intravenous injection is for any reason impossible, an injection deep into the gluteal muscle is more rapidly absorbed than a subcutaneous injection. He adds that high doses injected intravenously combine more surely with the toxins and are more apt to prevent paralytic complications.

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**Tuberculin Treatment Among Dispensary Patients.**—HAMMAN and WOLMAN (*Bull. Johns Hopkins Hospital*, 1909, xxi, 225) write concerning the tuberculin treatment of dispensary patients. They believe that tuberculin may be used in the dispensary without danger and with the most satisfactory control. All dispensary patients are not suitable for the tuberculin treatment. A degree of intelligence is essential, the patient must be willing to undergo a long and often tedious cure, and must be faithful in carrying out instructions. A certain amount of home comfort and enough leisure to allow regular attendance at the dispensary are required. The early cases are much more favorable for the treatment, but in their series Hamman and Wolman took all stages. Most of the women did some work at home, and some of the men worked more or less constantly throughout the whole period of the treatment. They furnished the patients with note books in order to be more sure of their coöperation. A visiting nurse to instruct and supervise the patients is essential. The patients were kept in bed whenever they had fever either occurring spontaneously or as a result of the tuberculin injections. Fever of a mild grade when other symptoms are favorable they do not consider a contra-indication to the treatment. In addition to the tuberculin the usual hygienic and dietetic measures were ordered. Some of the patients were given olive oil,

tonics, and a few had heroin and codeine for their cough, when severe. Hamman and Wolman believe that the potency of all the tuberculins depends upon the same substances and that all act in the same way. They used old tuberculin, new tuberculin, T. R., and the bouillon filtrate of Denys. Fresh dilutions were made every two weeks, and apparently the strength remained uniform during this time. They emphasize that the injection must be subcutaneous in order to determine any subsequent local reaction. They give the tuberculin in gradually increasing doses, as advocated by Trudeau, Denys, and Sahli. The initial dose is from 0.00000001 to 0.000001 gram. In the smaller doses they give injections twice a week; after 0.01 gram is reached only once a week. The essential feature of this method is to avoid the occurrence of any reaction and to carry the individual patient only as high as his tolerance will permit. The signs of developing intolerance may be expressed by a rise of temperature, constitutional symptoms, a local reaction at the site of injection, or a focal reaction, that is, an increase in the tuberculous process as measured by an increase in the physical signs or symptoms. After a moderately severe or severe reaction ten to fourteen days should elapse after all symptoms of the reaction has subsided, and then much smaller doses should be used. If a local reaction occurs the same dose is repeated until no local reaction occurs. If, on the other hand, the local reaction becomes more severe, the dose is decreased and then cautiously raised. The average maximum dose of tuberculin was 0.005 gram. The largest dose administered to an individual case was 1 gram. The early cases and those that do well take the largest dose. The far-advanced and progressive cases reach the limit of tolerance early. The duration of the treatment is based rather on the progress of the case than on the condition at the beginning of the treatment. The total number of patients who received the tuberculin treatment was 112. Hamman and Wolman report only those who were under treatment at least ninety days, a group of 71 cases; 14 of these 71 cases were not positively pulmonary tuberculosis, although probably so. They all improved as regards their tuberculous symptoms and the suggestive physical signs disappeared. The 57 remaining cases were divided into 13 incipient, 16 moderately advanced, 28 far advanced. Of the 57 patients, 10 were apparently cured, in 16 the disease was arrested, 12 were improved, 18 were progressive, and 1 far advanced case died. Of the 18 progressive cases, 4 improved as regards symptoms, 10 were unchanged as regards symptoms, and 4 far advanced cases were worse as regards symptoms. Of the 13 incipients, only 1 was progressive; of the 16 moderately advanced, 2 were progressive; of the 28 far advanced, 16 were progressive. The average gain in weight for the entire group was six and one-half pounds. The maximum gain in weight was forty-one pounds, and occurred in a far-advanced case.

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**The Lowering of Blood Pressure by the Nitrite Group.**—WALLACE and RINGER (*Jour. Amer. Med. Assoc.*, 1909, xx, 1629) have made some observations in order to determine the comparative effect of the most common drugs of the nitrite group upon the blood pressure of normal individuals and of patients with arteriosclerosis. In order to obtain uniformity of results they gave amyl nitrite in dosage of 3 minims by

inhalation; nitroglycerin, 1.5 minims of a 1 per cent. solution; sodium nitrite, 1 grain in solution; and erythrol tetranitrate, 1.5 grains in chocolate tablets. The latter three were given by the stomach. All of these drugs, in the doses above given, seemed to cause the same fall of blood pressure in normal individuals. The chief difference in their action lay in the rapidity and the duration of the fall of blood pressure. They found that the action of amyl nitrite began within one minute and was over within seven minutes; that of nitroglycerin began within two minutes, and was over within thirty minutes; that of sodium nitrite began within ten minutes, and was over within one hour; that of erythrol tetranitrate began within fifteen minutes, and was over within two to four hours. In general they found that the higher the initial pressure, the greater was the actual fall. Increase in dosage produced an increase in degree and duration of the action which is, as a rule, fairly proportional to the dose. In studying the effects on abnormally high blood pressures they took patients suffering from arteriosclerosis with pressures varying from 172 to 256 mm. Hg. They gave the following doses,  $\frac{1}{36}$  grain of nitroglycerin, 2 grains of sodium nitrite, and 2 grains of erythrol tetranitrate. On comparing the results obtained in normal individuals with the results in arteriosclerotic patients, they found them very similar. Nitroglycerin had the same effect upon arteriosclerotic patients as upon normal individuals. Sodium nitrite and erythrol tetranitrate acted a little less quickly, the maximum effect came a little later, and the duration of action was slightly longer than was the case with normal individuals. Wallace and Ringer obtained a fall of blood pressure in every case. They believe that the fall of pressure is due to a dilatation of the splanchnic vessels, and that a failure is due to the fact that the splanchnic vessels are no longer capable of dilatation. They also discuss the question of the best form in which nitrites should be given, and whether they deteriorate in activity by keeping. Amyl nitrite, as usually supplied in glass pearls, keeps well if not exposed to the light. Nitroglycerin tablets may retain their activity for a year or more. However, the content of nitroglycerin in fresh tablets may vary considerably, and it is best to make use of a solution of nitroglycerin. A 1 per cent. solution keeps fairly well, and is the most reliable as regards uniformity of strength. Solutions of sodium nitrite deteriorate rapidly. A solution should not be used which is over a week old. Matthew states that ordinary tablets of erythrol tetranitrate are usually inert, but that the full activity is retained by coating the tablets with chocolate. Wallace and Ringer have found that even after keeping for one year these tablets retain their full activity.

**The Treatment of Pertussis with Eucalyptus.**—SOLDIN (*Klin.-Therap. Woch.*, 1909, xxix, 722) says that eucalyptus leaves have been advocated for a long time in the treatment of various respiratory diseases, especially asthma and chronic catarrh. A disinfectant and a sedative action have been ascribed to the ethereal oil contained in the leaves. Danielus and Sommerfeld advocated the vaporization of the leaves in the treatment of tuberculosis. Other authors doubt its efficacy, but it does seem to diminish both the cough and expectoration. Soldin made use of two commercial preparations of eucalyptus leaves, sanosin and sydosin, in the treatment of pertussis. He treated 26 cases in all, and

found it lessened the number and severity of the paroxysms in most of the cases. Three of the patients failed to receive any benefit from the treatment. Soldin found that this treatment was of especial value when there was a marked bronchitis or when there were indications of a complicating bronchopneumonia. He does not believe that this method is specific, but thinks it does diminish the severity and length of the disease. He advocated its use because it may be given with perfect safety.

## PEDIATRICS.

UNDER THE CHARGE OF

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**The Treatment with Lactic Acid Bacilli of Infantile Diarrhœas Due to Intestinal Fermentation.**—C. H. DUNN (*Jour. Amer. Med. Assoc.*, 1909, liii, 5599) believes in an etiological classification of infantile diarrhœas. There are four fundamental etiological factors: (1) Nervous influences; (2) indigestion; (3) bacterial fermentation; and (4) bacterial infection. He states that true bacterial infection is caused by parasites, which live in and on the tissues of the body, whereas bacterial fermentation is caused by saprophytes living in and on the intestinal contents. The treatment of the two conditions is absolutely different, the former cases yielding to scrotherapy and vaccine therapy, the latter to other methods. Dunn quotes Tissier, who found that *Bacillus perfringens* is the cause of fermental diarrhœa, and that the lactic acid bacillus stopped its development. He, therefore, gave such patients pure cultures of this bacillus, noting rapid transformation of their stools, subsidence of their symptoms, and gain in weight. For this same purpose Dunn employed unpasteurized buttermilk, believing that it would contain large numbers of these bacilli. The buttermilk selected was first pasteurized to kill all other organisms, then inoculated with a pure culture of lactic acid bacilli, and ripened until the development of the organism had brought about the proper acidity and precipitation of the casein. Of 28 cases of fermental diarrhœa thus treated, 23 recovered completely, in 3 the treatment was partly successful, while in only 2 did it fail. The cured cases lost their diarrhœa, and gained weight rapidly. All these babies had failed to improve on routine treatment, and also when fed on pasteurized buttermilk; the recovery, therefore, cannot be due to the chemical peculiarities of the food, but to the only new element added, the lactic acid bacilli. In a number of the children, to assure a steady gain in weight, the patient had to be given alternate feedings of modified milk, thus suggesting that while buttermilk can check the fermentation, it is not suited to the caloric needs of the child. In all the cases the buttermilk was stopped as soon as the diarrhœa was checked, and the food employed previously was resumed. In four cases ripened milk could not be digested; they



were given pure cultures of lactic acid bacilli with excellent results. When pure cultures are added to modified milk, the success is much greater if all the fat has been removed from the milk previously. He concludes that the lactic acid treatment is of great value in fermental diarrhoeas, that it is not absolutely a specific treatment; the failures may be due to an ineffective lactic acid bacillus; it should be tried in every case of infantile diarrhoea characterized by saprophytic fermentation, and in every case of chronic intestinal indigestion and atrophy in which the movements show fermentation. A ripened milk containing living bacilli he considers the best food with which to begin feeding in cases of fermental diarrhoea after the initial period of starvation.

**Adenoid Hypertrophy during the First Year of Life, and its Treatment.**—R. G. FREEMAN (*Jour. Amer. Med. Assoc.*, 1909, liii, 605) emphasizes the following symptoms as pointing to the existence of adenoids: Snuffles, snoring, mouth breathing, recurrent colds, cough, and otitis media. He describes his method of examining infants for adenoids, and states that a chronic enlargement requires but one type of treatment—operative procedure. The operation in infancy can be done quickly without an anesthetic, with very little shock to the child and with no lasting fright. If an anesthetic is insisted upon, it should be nitrous oxide, and only primary anesthesia should be produced. The operation may be performed as early as the fourth to the fifth month.

**Suppurative Conditions in the Joint Regions in Infants and Young Children.**—L. E. LA FETRA (*Jour. Amer. Med. Assoc.*, 1909, liii, 608) comes to the following conclusions: (1) Cases of arthritis and of what might be called "near arthritis" are quite common in infants and young children. (2) In all cases a careful history of the infant from birth should be obtained. The inquiry should be directed particularly toward obtaining a history of umbilical infection, of early ophthalmia, of vaginitis, of pneumonia, typhoid, and influenza. (3) The feeding history, especially the use of sterilized, carbohydrate, or proprietary foods, should be carefully scrutinized. An inspection of the gums may save an incision into the thigh. It goes without saying that the patient should be undressed entirely for examination. Men frequently fail in diagnosis, not because they do not know, but because they do not see the patient, and do not make use of what they know. (4) The diagnosis of tuberculosis and rheumatism should be made by exclusion. (5) The earlier proper treatment is instituted the fewer the number of joints involved and the greater the chance of complete recovery of function. He advises dressings of aluminum acetate or of 60 per cent. alcohol in all early cases, but if progress is not satisfactory, the joint must be incised, evacuated and drained; if there is bone disease, the bone must be scraped. Vaccine therapy, especially the use of streptococcic and staphylococcic vaccine, is often a very valuable aid.

**The Secretion of Gastric Juice in the Pathogenesis and Course of Pyloric Stenosis of Nursing Infants.**—In contradistinction to other observers, ENGEL (*Deut. med. Woch.*, 1909, xxxv, 1271) believes the first change, and the most important probably, in the genesis of a stenosis of the

pylorus to be a secretory disturbance of the stomach. This is neither a hyperacidity nor a hyperchlorhydria, but rather a gastrosuccorrhœa, a formation of true gastric juice. The presence of gastric juice in the empty stomachs of nursing infants he considers a sign of disease. Simultaneous with this flow of gastric juice there is a spastic closure of the pylorus. Whether due to the same cause that induces the flow of gastric juice and occurring simultaneously, or whether occurring secondarily to it, cannot be definitely decided. The latter seems the more probable. After this acute stage of excessive secretion has passed off, a chronic and non-spastic narrowing of the lumen of the pylorus remains, and this disappears only very slowly. At this time signs of stasis make up the chief part of the clinical picture. The stasis of fat first pointed out by Tobler, is an especially characteristic sign of retention. The cause of the condition, therefore, lies in an extraordinary hyperexcitability of the gastric mucosa. Engel publishes the details of two cases, which form the basis for his conclusions.

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**Noma of the Ear, Terminating in Recovery.**—O. HOMUTH (*Deut. med. Woch.*, 1909, xxxv, 1276) reports the case of a child, aged fifteen months, in whom, for some time prior to the onset of measles, there existed a suppurative otitis media. Two weeks after the onset of measles the discharge from the ear became more marked and assumed a bad odor; a few days later an ulcer formed in the auditory canal and the auricle became necrotic. In the course of the next few weeks the gangrene continued to spread until the entire auricle had been removed, the middle ear cleaned out, and a part of the parotid gland cut away. The sudden appearance, the acute course, the absence of pain throughout, and the absence of syphilitic signs made a diagnosis of syphilis or tuberculosis, the only other diseases to be considered, impossible.

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**The Feeding of Immature and Atrophic Infants.**—Poor foetal development, according to A. G. SPALDING (*Jour. Amer. Med. Assoc.*, 1909, liii, 998), may be the result of heredity or of anemia or toxemia, such as is due to syphilis, alcoholism, poverty, gonorrhœa, nephritis, heart disease, and tuberculosis. Appropriate treatment of the mother during pregnancy may prevent an immature or atrophic state at the time of birth. Such infants are very much in need of mother's milk, as this possesses certain inherent properties, which aid the action of the "hormones," whose function it is to stimulate the different digestive ferments. If mother's milk is not available, feeding should be carried on with due regard to the avoidance of food intoxication, which favors failure of development; excess of fat is most likely to cause food intoxication. Spalding has devised a method, which is described by him in detail by means of a chart. It has been successful in his hands in the treatment of such infants; when he adds fats to the diet, he watches the infants carefully, reducing it at the first signs of indigestion.

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**Vaccine and Serumtherapy in Children.**—Vaccine therapy produces an active immunity to the specific bacteria, while serum therapy produces a passive immunity only. C. F. KERLEY (*Jour. Amer. Med. Assoc.*, 1909, liii, 1179) reveals the results of the two types of treatment in children: the former has given the better results in staphylococci

infections; the inoculations, varying from 7,000,000 to 50,000,000 of bacteria, depending upon the child's age, should be repeated every sixth to tenth day, the opsonic index being the criterion as to when the injection should be repeated. In furunculosis and acne excellent results have been obtained by this method of treatment. Streptococcic infections do not yield so readily; the injection dose is about one-third of the staphylococcic. The course of erysipelas is shortened by the injection of staphylococci; scarlet fever has not been influenced at all. In local streptococcic inflammations, such as adenitis, otitis, osteomyelitis, encouraging results have been obtained by the treatment. Gonococcic injections in vulvovaginitis have been without results, as have been pneumococcic injections in cases of pneumonia; but pneumococcic empyema has been distinctly improved by vaccine injections. Flexner's serum is of greater advantage in cerebrospinal meningitis than mere vaccination. Cystitis due to *Bacillus coli communis* is shortened by inoculations with dead colon bacilli. Tuberculin is of value in chronic local tuberculosis, without constitutional symptoms (bone, joint, gland, skin, and eye infections), and in chronic pulmonary tuberculosis; but in lesions associated with signs of fever, the injection of tuberculin is harmful.

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## OBSTETRICS.

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UNDER THE CHARGE OF

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**Methods of Operation in Deficient Dilatation of the Cervix.**—One of the last papers written by PFANNENSTIEL is upon this subject, published in *Monatschr. f. Geb. u. Gyn.*, 1909, xxx, Heft 5. He urges upon the general practitioner the use of elastic bags in cases in which dilatation of the cervix is not greatly hindered by the presence of scar tissue. Should this be present, he advises multiple incisions for 2 or 3 cm. When, however, the cervix has not been shortened, he would advise abdominal Cesarean section in cases in which the mother's life is threatened, as he considers this safer than the use of Bossi's dilator. When the mother's life is not in danger, and yet the indication is to dilate the womb and empty it, he prefers the use of bags to that of a metal dilator. He regards as especially demanding delivery, eclampsia, fever occurring during labor, and prolapse of the umbilical cord. In placenta prævia he states that the results of combined version have been a maternal mortality of from 9 to 10 per cent., and a foetal mortality of 81 per cent. to 62 per cent. in vigorous children. If an elastic bag be introduced through the placenta and then distended, delivery can be effected, with a maternal mortality of but 5 per cent., and from 25 to 42 per cent. mortality for the children.

He warns against active measures for delivery in patients that have

suffered from very severe hemorrhage, and would choose that method which would control the hemorrhage with the least disturbance to the mother. In many of these cases abdominal extirpation of the uterus gives the best chance. He compares them to ruptured ectopic gestation.

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**Acute Lysol Poisoning from Irrigation of the Uterus during Suprasymphyseal Cesarean Section.**—BIRNBAUM (*Zent. f. Gyn.*, No. 44, 1909) reports the case of a multipara with a flattened pelvis, who was operated upon by suprasymphyseal section. After the uterus was opened the child was readily delivered by external pressure. The amniotic liquid had an offensive odor, and after the placenta was delivered the uterus was irrigated with two quarts of 0.5 per cent. lysol mixture. The uterus was then sponged to remove the excessive fluid. There was no evidence that air entered the vessels at the placental site. While sutures were being introduced the patient's pulse became very slow, and the breathing slow, superficial, and attended with rales. Under massage of the heart and artificial respiration the patient's condition improved. Half an hour afterward the symptoms again appeared, and were followed by death. Postmortem examination was entirely negative. The heart muscle showed a very faint trace of fatty degeneration. The case is considered to be one of acute and fatal poisoning with lysol by the irrigation at the site of the placenta. It is thought that the raised position of the pelvis favored the accident and that it brought the fluid more immediately in contact with the upper portion of the uterine cavity.

This same coincidence has been observed in other cases in which intoxication with lysol occurred, the patient having been operated upon with the pelvis raised. This accident naturally suggests the caution that with patients in this position the uterus should not be irrigated, but if necessary should be sponged with sterile gauze.

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**The Interruption of Pregnancy for Pulmonary Tuberculosis.**—ALBECK, of Copenhagen, and RODE, of Christiana (*Zent. f. Gynäk.*, No. 44, 1909) contribute a paper upon this subject to the Norwegian Surgical Society in its gynecological section.

In Meyer's clinic in Copenhagen, 82 cases of pulmonary tuberculosis complicated by pregnancy had been observed; 28 of these had phthisis before the beginning of pregnancy, and the disease showed no increase during pregnancy; in the puerperal period 19 of these had fever, and with 4 the disease made evident progress. None of them died of the tuberculosis. Among the remaining 54 the first symptoms of tuberculosis appeared during pregnancy, or a previous infection became acute during this time; 15 of these died of pulmonary tuberculosis soon after delivery; 12 showed marked increase in the pulmonary lesions during the puerperal period; 11 among the 54 had tuberculosis of the larynx, and of these 6 died.

In a private sanitarium, 19 patients having tuberculosis were observed during the pregnant condition. Among these 16 were followed through pregnancy and the puerperal period, and of these it was found that 6 died within a year and a half after the birth of the children.

The tuberculosis seemed aggravated not earlier than the fifth month

of gestation. It was difficult to base a prognosis, as some patients did not seem at first to be unfavorably influenced by pregnancy.

As regards the influence of pulmonary phthisis in producing abortion, 1194 cases of early abortion were examined, and in none of them could phthisis be recognized as the cause. In 17 of the 82 cases studied, pregnancy went to within four weeks of full term. In the remaining 65 pregnancy went to the utmost limit.

So far as the children were concerned, 8 were stillborn—one from deformity, 3 because premature, and 4 after difficult delivery. While the mothers were in the hospital 4 others died; the remaining were discharged in good condition, and some of the children were above the average in weight and development. An effort was made to trace these children afterward, and 38 of them were followed through the first year of life; 13 of these died; the remaining 25 were healthy at the end of the first year.

The conclusion of these investigations seems to be that pulmonary tuberculosis rarely if ever causes abortion and very seldom brings on premature labor. Its effect upon the children seems to be less than many have supposed.

Moller had been averse to the interruption of pregnancy in cases of pulmonary tuberculosis, but the results of non-interference had been exceedingly bad. Not less than 58.3 per cent. of his patients died within a year after the birth of the children, and but 25 per cent. of them passed through labor without growing worse.

Of those becoming pregnant and having pulmonary tuberculosis, 50 per cent. died, or were made very much worse. This experience has led him to believe that pregnancy should be interrupted in this condition.

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**Suprasymphyseal Cesarean Section.**—RUNGE (*Archiv f. Gynäk.*, 1909, lxxxix, Heft 2) reports 22 cases of suprasymphyseal Cesarean section in Bumm's clinic. He considers Latzko's method to be more simple and practical than Sellheim's, and believes that by this method the danger of wounding the peritoneum is reduced to a minimum.

As an aid to recognizing the position of the bladder, a catheter may be introduced into the bladder before the operation. A transverse incision through the abdominal wall gives the best view of the field of the uterine opening. In 9 of the 22 cases the peritoneum was injured to some extent, and 8 of these were operations performed after Sellheim's method. There were small lesions of the bladder in 3 cases; 2 of these were Sellheim's operation and 1 Latzko's method.

The uterine cavity was opened by a longitudinal incision, but considerable hemorrhage from the uterine wound was not observed. It was not necessary to enlarge the uterine incision to extract the child.

In 14 cases the vertex of the fetal head presented; the forceps was used twice—once in abnormal presentation, and once in face presentation. In 4 cases in which the vertex presented the head could not be pressed down sufficiently for extraction, and version was performed. In one case the presentation was that of the breech and the feet. The forceps should not be applied until anterior rotation of the occiput has been performed by the hand, if necessary.

All of the children were delivered alive, some of them slightly asphyxi-

ated, but easily resuscitated. There were no complications in the delivery of the placenta, and in most cases the operator was not obliged to hurry this stage of labor. The placenta was expressed by Credé's method, or removed by the hand, as seemed necessary. In 2 cases the connective-tissue region of the pelvis was drained after operation, as in one case cocci and bacteria were found in the amniotic liquid. In 19 patients the puerperal period was without noticeable complications. In 6 patients pus formed in the abdominal incision; one of these patients suffered from pneumonia, bronchitis, and angina. In 3 patients there were severe complications during the puerperal period; one had phlegmonous inflammation of the connective tissue of the pelvis; and two of these patients died.

The mortality rate of the mothers was 9.1 per cent. Among these was one case of eclampsia. The mortality rate of the children was nil.

In 15 cases the patient was discharged with the uterus anteflexed and movable; in one patient anteflexion was present, but the uterus was adherent to the abdominal wall. This operation was performed after Sellheim's method, and was a difficult operation, with injury to the peritoneum. In one case there was complete retroflexion, and the cervix was adherent to the abdominal scar. This patient had phlegmonous inflammation of the pelvic connective tissue, but recovered.

At the time of writing, 2 cases were still under treatment, and 2 patients had died. There were some cases of hernia in the scar, adhesions to the anterior cervical wall and the abdominal wall, and the development of scar tissue in the connective tissue of the pelvis. As a rule, however, the results of the operation seemed favorable.

The question naturally arises, What would be the fate of such a patient in subsequent labor? The scar is left in that part of the uterus which is subjected to the severest pressure during parturition, and the natural fear would be that rupture of the uterus at this point might develop.

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## GYNECOLOGY.

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UNDER THE CHARGE OF

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**The Preparation and After Treatment of Celiotomy Cases.**—S. E. TRACY (*Surg., Gyn., and Obst.*, 1909, viii, 645) minutely considers the preparation and after-treatment of celiotomy cases, offering several valuable suggestions. One notable feature in Tracy's preparatory treatment is the careful inspection of the buccal cavity and prophylactic treatment of it. This consists in applying to the teeth and gums some preparation of silver in solution, followed by spraying under high pressure with full strength peroxide of hydrogen. Mouth cleansing is a feature of both the preparation and after-treatment. Tracy gives morphine and atropine

hypodermically an hour before the anesthetic is administered, but positively shuns the employment of these analgesics for postoperative pain. In the treatment of shock the remedies long discarded by many are still commended. Among these are alcohol, strychnine, etc.

**Cancer of the Cervix Uteri Following Subtotal Hysterectomy.**—REYMOND (*An. de gyn. et d'obst.*, 1909, xxxvi, 117) reports a case of cancer of the cervix following by some years a subtotal hysterectomy. Raymond found the cancer was so extensive that an abdominal operation seemed necessary and was performed for removal of the disease. The case was used as an argument for total instead of subtotal hysterectomy.

**Abnormal Secretion from the Mammary Glands.**—G. GELLHORN (*Jour. Amer. Med. Assoc.*, 1909, lii, 1839) holds that physiological experiments have demonstrated the specific function of the mammary gland is independent of the nervous system. But Gellhorn insists that certain moot questions concerning the functions of these glands require further careful observations. After referring to demonstrations of lacteal secretion occurring in pregnancy, the puerperium, the newly born, the growing child, the adult virgin, and the old woman, he offers reasonable evidence that it may be prolonged indefinitely after childbirth and may be associated with certain pathological conditions within the genital sphere. Aside from the intense scientific interest in the genesis of lacteal secretion, Gellhorn believes there is considerable practical importance attached to abdominal activity of the mammary glands, and a thorough knowledge of the atypical function of these organs is indispensable to the expert in medicolegal practice.

**The Significance of Peritoneal Adhesions Following Operations.**—H. T. BYFORD (*Surg., Gyn., and Obst.*, 1909, viii, 576), in his paper read before the American Gynecological Society, stated that much of the difficulty from peritoneal adhesions following operation is a result of "the postgraduate, looking on" course in general surgery, which is thought to be or pretended to be a sufficient preparation for an unlimited indulgence in peritoneal surgery, and, consequently, many operations for the relief of the adhesions resulting from such imperfect operations. Byford recommends the slightest amount of handling of the peritoneum and the frequent employment of drainage in pelvic operations, using either the abdominal or the vaginal routes. He prefers the glass tube for drainage through the abdominal wall and gauze for drainage through the vagina.

**Tuberculosis of the Gland of Bartholin.**—LECÈNE (*An. de gyn. et d'obst.*, 1909, xxxvi, 77) failed to find reported a single case of tuberculosis of the Bartholin gland in the literature of gynecology of the past twenty years, and attributes its great rarity to the absence of histological study of chronic inflammation of this structure. He refers to the case of tuberculosis of Cowper's gland found by Hartmann and himself in 1903, and Hallé's subsequent systematic examination of the specimens of Cowper's glands in the Museum of Guyon à Necker, which resulted in the discovery of tuberculosis in many specimens. He expresses his belief that the same result would be found with the specimens of Bar-

tholin's glands. Lecéne has observed two cases of tuberculosis of Bartholin's gland. The first was of a woman, aged forty years, on whom Dujarier did an abdominal hysterectomy, he having diagnosticated cancer of the cervix uteri. That diagnosis seems erroneous, as sixteen months later a nodule appeared on the labium that, on extirpation and microscopic examination, proved to be a tuberculous Bartholin gland. The second case occurred in a woman, aged twenty-three years, who applied for treatment of large masses in the groins. An ulcer was found in the vulva that involved a Bartholin gland and an anal fistula. Believing the vulvar ulcer was syphilitic, a bacteriological study revealed tuberculosis, and exsection of the pathological lesions in the three sites mentioned resulted in cure.

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**Local Anesthesia in Dilatation of the Cervix and in Cervical Operations.—**

OTTO HENRICH (*Zentralbl. f. Gynäk.*, 1909, xxxiii, 524) employs a 1 per cent. solution of  $\beta$ -eucaine to which sodium chloride and a trace of adrenalin has been added in producing local anesthesia in cervical dilatation and in operations on the cervix. The needle of the syringe is introduced into the cervical tissue for 1 to 1.5 cm., and while it is being withdrawn a few drops of the solution are injected. He makes four injections, and, finally, injects a few drops into the cervical canal. After waiting at least five minutes dilatation is effected without producing pain. He employed this method in a large number of cases with excellent results. No bad effects were observed. When larger doses are used the quantity should not exceed two syringefuls.

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**The Influence of Corsets and High-heeled Shoes on the Symptoms of Pelvic and Static Disorders.—**REYNOLDS and LOVETT (*Surg., Gyn., and Obst.*, 1909, viii, 569) have carefully studied the effects of corsets and high-heeled shoes on the symptoms of pelvic and static disorders, and the conclusions reached are at wide variance with the teachings for generations. After patient study a method has been devised for determining the centre of gravity in any living person in any position, and it has been found that many of the symptoms of pelvic and of static conditions are due to the centre of gravity of the body being too far forward. It is also believed that many times pelvic conditions, such as inflammatory states, adhesions resulting from infectious inflammation, or uterine or other neoplasms, bring about the gravity displacement. Wearing of badly fitting corsets is a prolific cause of it. The backache and headache of women is found to result frequently from this gravity displacement. Reynolds says most corsets do not fit properly unless made to order. It was found that a properly fitting corset not only is not harmful, but, *per contra*, puts the centre of gravity at the proper point, and relieves many of the symptoms thought to be due to gynecological ailments. Reynolds and Lovett also state that high-heeled shoes, while injurious to the feet, do not act injuriously upon the back as the centre of gravity, provided a properly fitting corset is worn at the same time.



## OTOLOGY.

UNDER THE CHARGE OF

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**Arterial Hypertension and Hypertension of the Labyrinth.**—LAFITE-DUPOND (*Annales des maladies de l'oreille, etc.*, December, 1908, p. 739), by experiments upon anesthetized dogs, determined the fact that an increased intralabyrinthine pressure was followed by an increase also in the arterial pressure. The increase in labyrinthine pressure was effected in some cases by increased air pressure in the tightly stopped external auditory canal, and in other instances by the injection of normal salt solution into the labyrinth itself through the medium of the round window, the increased or decreased pressure of the cerebrospinal fluid being accompanied by corresponding variations in the blood pressure. The channels of communication between the labyrinth and the cerebrospinal space are the aqueductus vestibuli and the nerve sheath of the acusticus; these, however, are so inadequate as a medium of gross communication, that a rapid translation of pressure from the labyrinth fluid into the cerebrospinal space cannot be conceived; but, as it was observed that the blood pressure changed almost instantaneously in response to the intralabyrinthine pressure, the inference is at least permissible that the internal ear is an organ with a capacity to exert an influence on the blood pressure. The pathogenesis of increased intralabyrinthine pressure is a difficult question. If the hypertension in the labyrinth stands in relation to increased blood pressure, which pressure is primary and which the sequence of the other? Lafite-Dupond has observed that in all patients with labyrinthine hypertension increased blood pressure was observable, as contrasted with the fact that with a considerably increased blood pressure there was no evidence whatever of disturbance of the auditory function, with the exception of a decrease in the upper tone limit of audition, and a shortening of the duration of hearing by bone conduction. The symptoms accompanying, in a greater or less degree of severity and frequency, the labyrinth hypertension are subjective noises, disturbances of audition, otalgia, diminished hearing by bone conduction, and increased blood pressure, these symptoms being sometimes accompanied by headache and vasomotor disturbances. For local treatment the author recommends massage of the drumhead, with short excursions of the piston of the air pump, and for general treatment the subcutaneous administration of pilocarpine.

**The Monochord and the Upper Tone Limit.**—R. WILBERG (*Archiv f. Ohrenheilkunde*, 1909, lxxx, 83, 165) states that the first recorded investigations, as to the upper tone limit of audition, made by means of the monochord, were those of F. A. SCHULZE (*Annales de physiologie*, 1907) and J. HEGENER (*Deut. Otol. Gesellsch.*, 1908) both observers

making individual tests in comparison with the Galton whistle, tuning forks,<sup>1</sup> and metal rods, preferentially in favor of the monochord as a controllable and reliable means of upper tone production. This instrument, as described by Schulze, consists of a length of slender steel or silver wire, preferably the former, fastened firmly at the two ends by means of clamps, and with an intermediate, movable clamp permitting definition of the vibration length of the wire, the production of the desired tone being effected by means of light longitudinal friction. For this actuation Schulze employed a small piece of leather, but Wilberg obtained better and more uniform results by the use of a wash leather glove, stroking the wire between the fingers, and later by using a strip of leather with a fish-tail slit in the end, the leather being drawn lengthwise of the wire with the apex of the slit rubbing upon the metal. The comparisons drawn between the test made with the monochord, and those including the upper limits of the Galton whistle served to confirm previous opinions in regard to the unreliability of the upper portions of the Galton scale, and emphasized the value of the monochord in such investigations as those undertaken by Wilberg to determine the upper tone limit of audition at different ages in the human subject. The conclusions drawn were to the effect that there is no generally determinable upper tone limit, that it is dependent upon the age of the individual and the strength of the tone employed, and that it is increased by accustomed use and decreased by conditions which represent a resistance to the passage of the sound waves, such as are presented in disturbances of the sound-transmitting apparatus.

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**Resistance Capacity of the Facial Nerve.**—R. BARANY (*Archiv f. Ohrenheilkunde*, 1909, lxxx, 147) states that in a case of mastoiditis, in a tuberculous subject, without evidence of the implication of the facial nerve, an operation resulted in the removal of a large sequestrum, including the whole of the tip of the mastoid process and the anterior and inferior walls of the osseous external auditory canal, including the stylomastoid foramen. At but one point, in the lower portion of its course, was the facial nerve surrounded by normal bone, but, notwithstanding the extent of the sequestrum formation, the nerve was functionally intact. In the discussion which followed the report of the case here recorded, G. Alexander drew attention to the fact that the facial nerve is especially resistant to such injury as might accompany hemorrhage, contiguous inflammatory processes, the pressure incident to cholesteatoma formation, or the effects of a surrounding bony necrosis, the vestibular nerve being less resistant than the facial, and the first nerve to suffer injury being the cochlear branch. H. Frey reported a case of carcinoma in which the facial nerve was almost completely embedded in the growth without evidence of loss of function, and F. Alt reported the removal, as a sequestrum, of almost the entire labyrinth, in the course of a radical operation, in a case in which there had been but slight evidence of facial paralysis. According to H. Neumann the reason for the greater resistance capacity of the facial nerve was to be found not only in its structural characteristics, thicker fibers, and larger nerve cells, but also in the fact that its blood supply being derived from the stylomastoid artery, the labyrinth drawing its main supply from the internal auditory.

# PATHOLOGY AND BACTERIOLOGY.

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**The Blood-pressure-raising Substance of the Kidney.**—A. BINGEL and E. STRAUSS (*Deut. Archiv f. klin. Med.*, 1909, xcvi, 476) report their careful observations on the blood-pressure-raising substance in the kidney in an interesting article. Tigerstedt and Bergman had previously shown the presence of a substance in watery extracts of rabbits' kidneys called rennin, which, when injected into rabbits, had a distinct blood-pressure-raising effect. Bingel and Strauss in their experiments used the pressed juice of fresh kidneys. Only the cortex corticis was employed, the pyramids being cut away and all blood washed out. The present investigation was carried out chiefly with extracts of pigs' kidneys, for Bingel and Strauss had previously shown that the extracts from kidneys of all large animals possessed the same effect, when injected into rabbits, as the extract from the kidneys of rabbits themselves. Tests were made with the juices of many other organs, but all save the hypophysis cerebri and adrenal gave depressor effects. The pancreas was especially noticeable in this respect. The action of the kidney juice was very powerful, for it produced a rise in pressure of from 40 to 60 mm. Hg. This lasted from one-quarter to one-half hour, and the descent was slow. Bingel and Strauss, moreover, were able to separate the active principle, which they call rennin, from the kidney extracts. Among other qualities they state that the activity of the substance is destroyed by heating to 58° C. and by the action of acids, alkalies, alcohol, and acetone. Physiologically it has precisely the same action as the whole kidney juice. After injection the effect is not immediate, but appears in about one-fourth of a minute. The rise in pressure is not extremely rapid, for it takes from one to two minutes to reach the highest point. The height is maintained for variable lengths of time and then there follows a gradual sinking in pressure. This decline usually requires from one-half to three-fourths of an hour. The maximum rise recorded in any of their experiments was 70 mm. Hg. A comparison of the action of rennin with that of adrenalin indicates that the former causes a much less sharp rise of pressure and permits a slower fall. Repeated injections of rennin produce progressively less effect, until finally there is no response. But this is not because the animal's blood-pressure-raising capacity is lost, for injection of adrenalin after a series of rennin injections causes prompt rise of pressure. If the animals are allowed to rest after such a series of rennin injections for two hours, the substance again provokes a rise of pressure. A curious phenomenon was noted when an animal was first injected with the juice of other organs and then

given rennin. No rise in pressure occurred. Cutting off the nerve control of the vascular system did not check the action of rennin. In conclusion the authors say that the action of rennin, like that of adrenalin, is exerted on the muscles of the peripheral vessels. They further suggest the possible significance of rennin in connection with the high arterial tension of kidney disease, especially with the sclerotic type of kidney.

A few months before the publication of the above paper the work of PEARCE (*Jour. Exper. Med.*, 1909, xi, 430) upon a similar problem appeared. He found, rather in contradiction to Bingel and Strauss, that injections of extracts of rabbits' kidneys caused in rabbits a very slight rise in blood pressure; extracts of dogs' kidneys caused in dogs a marked fall in pressure; while extracts of cats' kidneys produced in cats a decided rise. Thus, each animal reacted differently to injections of extracts of kidneys of the same species. It was found, besides, that each animal always reacted in the same way toward kidney extracts of other species. Thus, dog's kidney extracts caused a slight rise of pressure in rabbits, while rabbit's kidney extracts produced a marked fall of pressure when injected into dogs. The extracts of kidneys which are the seat of experimental nephritis do not differ from those of normal kidneys. The serum, however, from dogs and rabbits which are the subjects of experimental uranum and chromate nephritis contains substances which cause some disturbance in blood pressure, evidenced either by a rise or fall when injected into other animals.

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**The Influence of Coronary Disease on the Heart Muscle, with Especial Reference to Chronic Aortitis.**—There has always been discussion as to whether the coronaries were true end-arteries or whether they anastomosed. Even after Lanzer's work in 1880 arguments were still advanced to uphold Cohnheim's view that the coronaries are end-arteries. Very closely dependent upon this anatomical point is the relation of coronary disease to the condition of the heart muscle, and VON REDWITZ (*Virchow's Archiv*, 1909, cxvii, Heft 3) reports a series of 18 carefully studied cases to show that heart muscle changes are rarely dependent upon disease of the coronary arteries. As an introduction, von Redwitz describes at length the vessels under discussion from an anatomical standpoint, and presents very satisfactory proof by means of ligature and injection experiments that there is a free anastomosis between the right and left coronary system and the vasa vasorum of the aortic bulb. Following this the work of Kolster is quoted to show that sudden blocking of a small branch caused, first, coagulation necrosis of heart muscle cells, and later a typical scar formation in the area supplied by the plugged branch. The resultant condition is infarction, but has been erroneously called myocarditis and grouped with that condition. The 18 cases could be divided, anatomically speaking, into two groups. In one the arterial disease was almost entirely or entirely confined to the bulb of the aorta, and affected the coronaries only by narrowing or closing their ostia. In the other group of cases the coronary arteries themselves were the seat of sclerotic changes of various degree and extent. Sections taken from different parts of the heart muscle almost always revealed numerous scar-like masses composed of fibrous tissue, small, round cells, and often larger epithelial

cells. Frequently fatty degeneration involving more or less of the organ was met with. But in only three cases could von Redwitz note any definite relation between the diseased coronaries and the distribution of the scars. For example, in one case in which both coronaries were equally diseased there were muscle changes in the region of the left apex only; in another, one coronary was completely blocked and the scars in the musculature were found distributed through the whole heart; in still others with advanced coronary disease there were no muscle changes. But it is interesting to note that in this last group a widely dilated epicardial capillary network continuous over the base of the aorta bespoke the activity of the auxiliary collateral circulation. The scars in the three cases, which were evidently due to closure of a small branch, von Redwitz believes to have been caused in the manner described by Kolster. To explain the pathogenesis of the myocardial changes in the absence of sufficient cause by coronary disease von Redwitz advances the following argument: A review of the other pathological conditions present in his 18 cases shows that 9 had marked valvular disease, 2 had aneurysm, 3 nephritis, and the remaining 4 advanced general arterial sclerosis. In other words, the myocardial changes were found in hearts which during life had been subjected to an undue amount of work, or had been injured by rheumatism.

**Protozoa in the Blood in Typhus Fever.**—KROMPECHER, GOLDZIEHER, and ARGYAN (*Zent. f. Bakt.*, 1909, 1, 619) had an opportunity during an epidemic of typhus fever in Budapest to study 48 cases during life. In the blood of all of these patients structures which simulated parasites were found. These bodies were present both inside the red blood corpuscles and free in the plasma. They were very scarce and could only be demonstrated by the Giemsa stain. Three types of structure are described, but in general these types were similar and consisted of a pale blue ground work containing red chromatin bodies. Although they were found in very small numbers, they could be seen constantly in daily examinations of the blood of patients during the illness. In the fatal cases at autopsy these same structures were seen in smears from the bone marrow and spleen, but in no other situation. They could not be demonstrated in sections. They resembled in form more closely piroplasma than malarial parasites. The authors believe that they can exclude the possibility of these bodies being artefacts from a precipitate or stain, blood platelets, nuclear products, or the metachromatic substances of red cells, and consider them parasites connected in some way with the disease.

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ORIGINAL ARTICLES.

**CONGENITAL SINGLE KIDNEY, WITH THE REPORT OF A CASE;  
THE PRACTICAL SIGNIFICANCE OF THE CONDITION,  
WITH STATISTICS.\***

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THE subject of "single kidney" is admittedly of considerable surgical and anatomical importance, but it is also one of decided interest to the internist and pathologist. The condition was known to and imperfectly described by some of the early writers, more particularly Vesalius and Eustachius. Various classifications of "unsymmetrical kidney" have been proposed—first by Morgagni in 1769, and later by Rokitansky, Morris, and other writers. These have, as a rule, included cases in which one kidney is merely atrophied as the result of disease, or undeveloped, and also the instances due to a fusion of the two organs. I have, however, discussed here only cases in which one kidney is entirely and congenitally absent. All those instances in which any rudiments or remnants of renal structure were detectable in the situation of the kidney have been omitted from consideration.

As regards the frequency of occurrence of the condition, there is marked diversity of opinion among writers. According to MacDonald Brown,<sup>1</sup> cases of single kidney are exceedingly rare. For example, in nearly 12,000 autopsies made in the various London hospitals prior to 1893, only 3 cases were found. He continues:

\* Read at a meeting of the College of Physicians of Philadelphia, December 1, 1909; and in a modified form at a meeting of the Luzerne County Medical Society, Wilkes-Barre, Pa., November 24, 1909.

"Indeed, only slightly over 100 cases have been recorded altogether, and even many of these were doubtfully true 'single kidney.'" Morris<sup>2</sup> observed but 2 cases in 8069 cadavers, Sangalli<sup>3</sup> 3 cases in 5348 necropsies, Menzies<sup>4</sup> 2 cases in 1790 sections, Petersen 1 case in 1500, Camargo<sup>5</sup> 2 cases in 3000, Owtschinniskow<sup>6</sup> 1 in 3800, White and Martin (quoting Mawkiewicz<sup>7</sup>) 1 in 3992, and Rootes<sup>8</sup> 1 instance in 600 autopsies. Ballowitz<sup>9</sup> prosected 617 bodies (of which 121 were females), and found 1 example of "single kidney" associated with defective development of the genitalia of the same side. He also observed 2 additional cases through the courtesy of his colleagues. Preindelsberger<sup>10</sup> found 2 instances of "single kidney" in 1344 sections, Reinfelder,<sup>11</sup> in the Munich Pathological Institute, met with 1 case in 400 autopsies, and Winter's<sup>12</sup> statistics show 13 cases out of 32,415 sections. Heiner<sup>13</sup> (through the courtesy of Dr. Sternberg) presents the figures of the Prosector at Brunn. Out of 8853 sections, from 1895 to 1905, 3 cases of asymmetrical kidney were found. Again, of 2145 sections, from 1906 to February, 1908, two subjects showed total absence of one kidney.

Among American authors, I find Weir<sup>14</sup> contending that single kidney occurs only once in 5000 subjects, and Guiteras<sup>15</sup> found, on analyzing a table of 15,904 autopsies, that in four cadavers there was absence of one kidney, that is, complete absence of one organ in about 4000 instances. Says Dennis,<sup>16</sup> according to available statistics, complete absence or extreme atrophy of one kidney is found once in 2650 cases. The statistics obtained from the records of routine postmortem work in certain leading hospitals of Philadelphia give somewhat similar results. For example, at the Pennsylvania Hospital 1 case was met with in 1250 postmortems; in 600 necropsies conducted at the Protestant Episcopal Hospital by Dr. William Egbert Robertson no case of the sort was encountered. Dr. C. Y. White informs me that he has not met with a single case of complete absence of one kidney in a personal experience covering 1800 autopsies. On the other hand, the records of the Philadelphia Hospital furnish 8 cases out of a total of 6240 autopsies (see table).

Moore<sup>17</sup> (in 1898) found, in averaging certain previous statistics that the "expectation" of "unsymmetrical kidney" was about 1 in 2400 autopsies. The aggregate of the foregoing figures, together with those accessible among the hospitals of Philadelphia, at the present writing, or a grand total of 92,690 postmortems, gives a ratio of 1 in 1817 autopsies.

The precise number of cases of congenital single kidney recorded in literature, answering to the definition given above, remains somewhat in doubt on account of the vague character of the reports of some of the earlier writers. Ballowitz,<sup>18</sup> in 1895, collected from the literature 210 cases, which, in addition to 3 observed by himself, gave a total of 213 cases. Moore, in 1898, published 12 additional references, and thus brought the total number up to 225

cases in that year.\* The two writers last cited (like myself) aimed to exclude those instances of "unsymmetrical kidney" in which the organ was much wasted as the result of disease processes, was undeveloped, and those resulting from fusion of the kidneys. Radasch,<sup>19</sup> in 1908, wrote: "If we accept 240 cases up to the appearance of Ballowitz's paper, then at least 15 more must be added, making a total of at least 255."

I have endeavored to collect the cases of genuine "single kidney" to be found in the literature since the publication of Moore's article in 1898 (a considerable number having escaped the scrutiny of more recent writers), together with a few scattered earlier cases, with a view to showing the grand total of all recorded instances of the condition to date. With the kind aid of my associate, Dr. H. Leon Jameson, I have found in accessible literature and the autopsy records of certain Philadelphia hospitals no less than 61 genuine cases, making the sum total to date 286 cases. These are reasonably accurate figures, and in future the number of cases belonging to this category need not remain in doubt, since the reports will doubtless be far less ambiguous than those of the earlier writers. I consider it to be a matter of considerable importance to have secured statistics, the results of an analysis of which point to definite conclusions, both as regards the question of "expectation" and that of the pathological and practical bearings of "single kidney." A consideration of the figures given in the accompanying table, in which 61 instances of the condition are detailed, will show interesting results. Before attempting an analysis of the tabulated list of cases, however, I shall give the notes of a case personally observed, together with various conclusions to which they point:

W. B., aged sixty-four years, a varnisher, a native of England, weighing 160 pounds, and five feet eight inches in height, was admitted to the Medico-Chirurgical Hospital April 10, 1909. The family history was good, except that his father died, at sixty-four years of age, of Bright's disease, and one brother at the age of sixteen, suddenly, but of unknown cause.

The patient had had all of the commoner childhood's diseases, including scarlatina; subsequently he continued well until eight or nine years ago, when rheumatism developed; it was of a subacute type and did not confine the patient to bed; he has had several recurrences of a similar nature during the past eight years. Last July one year ago, while working at his trade, his right arm, from elbow to finger tips, particularly on the ulnar side, as well as his right leg, from the knee down to the toes, manifested a sense of numbness, which, however, passed away in the course of fifteen minutes. Last July he had a similar attack, which left his hand in a drawn or partially closed condition; it is now straightened out, except that his middle finger is still distinctly contracted.

\* This writer actually published 13 references, but one was a report of a horseshoe kidney, hence omitted.

Reporter	Age and sex	Which absent	Ureter	Renal artery and vein	Corresponding suprarenal	Condition of genitalia	Condition of existing kidney as to size, shape, position, and lesions present.
Darby <sup>22</sup>	60 yrs.; female	Left	.....	Absent	Absent	.....	Kidney healthy; carcinoma of bladder and lungs.
Isaacs <sup>21</sup>	3 mos.; male	Left	Absent	....	Present	.....	About twice natural size, 2¾ x 1¼ x 1¼ in.; lobulation characteristic of infantile kidney; healthy; deceased of pneumonia.
Turner <sup>22</sup>	Past middle life; female	Left	.....	Absent	Present	Uterus unicornus	Not hypertrophied; no lesion.
Wier <sup>22</sup>	Male	Left	Absent	....	.....	.....	Enlarged, 5 oz., 2 drams; normal, healthy.
Ingals <sup>24</sup>	Middle aged; male	Right	Lower end dwindled for 4 in.	....	.....	.....	Normal size, roughened surface, pale and hard, cortical substance thick; contained two cysts.
Fenby and Walker <sup>25</sup>	... female	Right	.....	....	.....	.....	Enlarged, weighing 9½ oz.
Peabody <sup>25</sup>	21 yrs.; female	Left	Absent	Two right arteries; none on left	Present	Uterus bicornate; right side better developed	Normal situation, double normal size.
Peabody <sup>27</sup>	61 yrs.; male	Right	Absent	Two renal arteries to left kidney; none on right	Present; normal	Normal	Double usual size, capsule of Bowman thick; interstitial inflammation; small hemorrhagic infarction.
Church <sup>23</sup>	45 yrs.; female	Left	Absent	Absent	.....	.....	Very small, not larger than a large hen's egg and shaped much like one; shows interstitial nephritis.
Church <sup>23</sup>	65 yrs.; male	Left	.....	....	.....	.....	Very large and healthy; deceased of gastric carcinoma.
Ebstein <sup>20</sup>	21 yrs.; female	Right	Absent	....	.....	Right cornu of uterus absent	Chronic pyelitis and chronic interstitial nephritis.
Smith <sup>20</sup>	33 yrs.; male	Left	.....	....	.....	.....	Enlarged, weighing a little more than 7½ oz.
Hand <sup>21</sup>	...	Right	Absent	....	Present	.....	Compensatory hypertrophy; patient had lumbo-sacral meningocele.
Murray <sup>22</sup>	8 yrs.; male	Right	Absent	Two small vessels from bifurcation of aorta	.....	.....	Large kidney, dilated pelvis; impaction of ureter with calculus; situated in hollow of sacrum behind bladder, more to left than right.
Lohsse <sup>22</sup>	Adult; male	Left	Absent	....	.....	.....	Considerably hypertrophied, otherwise shows no pathological change.
Israel <sup>24</sup>	52 yrs.; male	Right	Absent	Artery absent	.....	Testicle 2 cm. long; is in pelvis	Enlarged, 12 cm. x 8 cm. x 6½ cm.; in normal position.
Bauer <sup>22</sup>	22 yrs.; male	Left	Absent	Present, but very small; vein absent	Present; and normal	Left vas deferens and seminal vesicle absent	Slightly enlarged, weight 190 gms.; normal position and form.
Francois-Dainville <sup>23</sup>	...	Right	.....	....	.....	.....	Very large, weighing 430 gms.; surface lobulated, somewhat congested.
Beaufume and Carron <sup>27</sup>	47 yrs.; male	Right	Absent	....	Right absent; left weighed 9 gms.	Right testicle small but appears sound; left in inguinal canal and is markedly atrophied	Weighs 250 gms., structure unaltered; normal situation; associated with total inversion of the viscera.

Reporter	Age and sex	Which absent	Ureter	Renal artery and vein	Corresponding suprarenal	Condition of genitalia	Condition of existing kidney as to size, shape, position, and lesions present.
Guiteras <sup>38</sup> (Case I)	21 yrs.; male	Right	Absent	....	.....	.....	5 x 3 x 2½ in.; lobulated, had but one pelvis; showed evidence of tuberculosis and nephritis.
Guiteras <sup>38</sup> (Case II)	30 yrs.; male	Right	Absent	....	.....	.....	7½ x 4 x 2½ in.; not distinctly lobulated, but somewhat irregular on surface; normal position; acute parenchymatous nephritis.
Guiteras <sup>38</sup> (Case III)	25 yrs.; male	Left	Absent	....	Absent	.....	4 x 2½ x 2 in.; five or six irregular elevations on its surface; somewhat lobulated; single pelvis; chronic interstitial nephritis.
Wilson <sup>39</sup>	55 yrs.; female	...	Two ureters from kidney	....	.....	Some malformation of uterus	Great size; no lesions.
Crawford <sup>40</sup>	62 yrs.; female	Right	Absent	....	.....	.....	"Large white" kidney; cicatrix in lower pole, result of previous tumor growth (died in coma).
Nelson <sup>41</sup>	20 yrs.; female	Right	Present; 3¼ inches long; closed at upper end	....	Both present and enlarged, especially right	Normal	Relation of vessels normal.
Brinkman <sup>42</sup>	Adult; male	Left	Absent	....	Absent	Left testicle and epididymis small	Decidedly enlarged; 16.5 x 7.5 x 5.5 cm.
Winter <sup>43</sup>	21 yrs.; male	Left	8 cm. long; occluded above	....	Present	Normal	One large and numerous little cysts; little normal kidney structure remaining; death due to nephrectomy.
Edington <sup>44</sup>	2 days; male	Right	.....	Absent	Present and normal	Right vas and epididymis small	Good size, 5 x 3 x 2 cm.; normal shape, though marked lobulation; normal position shows cloudy swelling; atresia anus and hare lip.
Moore <sup>45</sup>	35 yrs.; male	Right	Absent	Absent	Absent; left present and normal	Normal	Considerably enlarged, 285 grams; normal position.
Moore <sup>45</sup>	50 yrs.; male	Left	Absent; right normal	Absent; right normal	Absent; right normal	Absence of genital apparatus on left side	Much enlarged, 480 grams; marked lobulation, otherwise normal in shape; normal position; patient had diabetes and gangrene; died of pneumonia.
Mori <sup>46</sup>	88 yrs.; male	Left	Absent	Artery absent	.....	.....	Large, 16 x 6 cm.
Robinson <sup>47</sup>	...	Left	Absent	....	.....	.....	Compensatory hypertrophy, being one-third excessively developed; normal shape.
Horrand <sup>48</sup>	7½ mos.; male	Right	Present; crossed median line and joined left before entering left ureter; was permeable	Absent	Present	Right testicle found in inguinal canal	Lobulated and hypertrophied.
Viannay and Cotte <sup>49</sup>	60 yrs.; male	Right	Absent	Absent	Both present	Absence of right vas deferens and vesicula seminales and corresponding ejaculatory duct; right testicle small; right lobe of prostate somewhat smaller	Compensatory hypertrophy, 250 gms.; normal situation.

Reporter	Age and sex	Which absent	Ureter	Renal artery and vein	Corresponding suprarenal	Condition of genitalia	Condition of existing kidney as to size, shape, position, and lesions present.
Delearde <sup>59</sup>	Young infant	...	.....	....	.....	.....	.....
Hollopeau <sup>61</sup>	50 yrs.; male	Right	Lower portion present, 13 cm. long; permeable and ends in blind pouch above	....	Present and apparently normal	.....	Normal situation; a little larger than normal.
Manson <sup>62</sup>	59 yrs.; male	Right	Absent	....	.....	.....	Large, weight 9 oz.; no pathological change.
Codina <sup>63</sup>	80 yrs.	...	.....	....	.....	.....	Abnormal form and situation; kidney showed changes of chronic nephritis.
Scheuer <sup>64</sup> (Case I)	3½ yrs.; female	Left	Absent	Absent	Present	Normal	Kidney showed amyloid change.
Scheuer <sup>64</sup> (Case II)	60 yrs.; male	Right	Present; and permeable for 1¼ cm., otherwise absent	Artery absent	Present; normal size and situation	Normal	Very much enlarged; on section, cortex found to be thickened; capsule stripped easily.
Scheuer <sup>64</sup> (Case III)	26 yrs.; female	Right	Absent	Absent	Present	Right ovary missing; bicornate uterus, septum extending into bladder	Enlarged, 15 cm. long; capsule adherent; numerous abscesses of kidney, ureter, and bladder.
Scheuer <sup>64</sup> (Case IV)	19 days	Right	Absent	....	Present	Atresia of urethra and anus	Much enlarged, partly due to hyperplasia and partly to hypertrophy.
Broek <sup>65</sup>	Adult; male	Right	Absent	Artery present; vein absent	Present	Absence of testicle, vas deferens and seminal vesicle; right lobe of prostate atrophied	Increased in size, 15 x 8 x 4 cm.; normal position.
Diamantis <sup>66</sup>	60 yrs.; male	Left	Absent	Artery absent	Present and normal	.....	160 gms.; surface smooth and regular.
Jacquin and Marquez <sup>67</sup>	57 yrs.; female	Right	Absent	....	Absent; left hypercystic	Lateral version	Weight 300 gms.; lobulated; normal position; evidence of chronic nephritis.
Schmidt <sup>68</sup>	64 yrs.; male	Right	Absent	Absent	Present	Right testicle and epididymis smaller; right seminal vesicle enlarged and is seat of round and spindle-cell infiltration; no spermatozoa present	Shows enlargement, 15 x 6¼ cm.; normal situation; no histological change.
Heiner <sup>69</sup>	40 yrs.; male	Left	Absent	Absent	Present	Tail of epididymis, vas deferens, seminal vesicles and ejaculatory ducts missing on right side; otherwise normal	Slight increase in size due to compensatory hypertrophy; 270 gms.; normal form and situation.
McCrae <sup>69</sup>	49 yrs.; female	Left	Absent	....	.....	Left ovary, tube, broad ligament and left half of uterus absent	Larger; normal position.

Reporter	Age and sex	Which absent	Ureter	Renal artery and vein	Corresponding suprarenal	Condition of genitalia	Condition of existing kidney as to size, shape, position, and lesions present.
Readue <sup>61</sup>	17 mos.; male	Left	Absent	....	Present; in normal position and form	Normal	Enormous compensatory hypertrophy; $6\frac{1}{2} \times 5 \times 4$ cm.; weight 85 gms. (normal 40-45 gms.); globular shape; no macroscopic lesions.
Orbison <sup>62</sup>	31 yrs.; male	Left	Could be traced upward from bladder for a few inches; enlarged	....	Present; measured $2\frac{1}{2} \times 1\frac{1}{4}$ in. and was flattened; right like left	....	No note of vessels; kidney $7\frac{3}{4} \times 2\frac{1}{8}$ in.; chronic interstitial nephritis.
Mackie <sup>63</sup> (Case I)	9 mos.; male	Left	.....	.....	.....	.....	Weighted 298 gms. and showed fatty change.
Mackie <sup>63</sup> (Case II)	7 mos.; male	Left	Absent	Absent	Absent	.....	Twice normal size, normal shape.
Mackie <sup>63</sup> (Case III)	44 yrs.; male	Left	Absent	....	.....	.....	Large, soft; shows tubercular disease.
Mackie <sup>63</sup> (Case IV)	34 yrs.; female	Right	Absent	Absent	Absent	Both ovaries are fibroid; small fibroid nodules in broad ligament	185 gms.; shows foetal lobulation, is ellipsoidal; shows some fibroid and fatty change.
Mackie <sup>63</sup> (Case V)	53 yrs.; male	Right	Exists for most part as fibrous cord; patulous for 4 cm. from bladder	....	Normal	.....	Very much enlarged, marked lobulation; shows changes of chronic nephritis.
Mackie <sup>63</sup> (Case VI)	49 yrs.; male	Left	Absent	Absent	Normal	.....	$11.5 \times 5 \times 3.5$ cm.; distinct foetal lobulations; evidence of chronic nephritis.
Mackie <sup>63</sup> (Case VII)	63 yrs.; male	Right	Absent	Both absent	Present; enlarged and softened	.....	Usually thick; $13.5 \times 4.5 \times 4.5$ cm.; shows chronic interstitial change with anemic infarct.
Mackie <sup>63</sup> (Case VIII)	40 yrs.; female	Left	Absent	....	Present	.....	16 cm. in length; pushed upward and forward and is firmly adherent to under surface of liver and diaphragm; shows extensive chronic diffuse nephritis.
Hagner <sup>64</sup>	40 yrs.; female	Right	Absent	Absent	Absent	.....	Kidney large, pyonephrosis.
Guthrie and Wilson <sup>65</sup>	30 yrs.; female	Left	Absent	....	.....	Left tube, broad ligament and ovary absent; cervix closed; hematometra; lower end of vagina absent; coitus through urethra	Diagram shows remaining kidney in normal position; size and condition not described.
Anders	64 yrs.; male	Left	Absent	Absent	Left absent; right hypertrophied	Normal	Hypertrophied; weight, 240 gms.; surface lobulated, in normal situation; evidence of chronic interstitial nephritis.

The patient is married, has three children, and up until three years ago he was a hard drinker, using on the average about a quart of whiskey and four or five pints of beer daily; otherwise, the social history is without significance.

The present illness began in October, 1908, at which time he noticed shortness of breath and pain across his chest upon exertion; he was easily exhausted, and complained of being constantly tired.



Out of the left eye objects appeared black, and about this time he was compelled to quit work on account of weakness and a feeling of exhaustion. During the previous month, and even subsequently, he passed large quantities of urine (about one gallon per day). In March, he had suffocating attacks, especially at night, and went to the Johns Hopkins Hospital as a patient. Here he was told that he had kidney and heart disease, and remained about five weeks.

*Physical examination* revealed a middle-aged white male, conscious, rational, though with tendency to stupor, falling asleep during examination; the skin was livid, being especially cyanosed over the extremities; mucous membranes also cyanotic; marked œdema of the ankles and feet, with slight wrist-drop of right arm; head and eyes normal, but nose cyanosed and cutaneous veins engorged; no teeth in upper jaw and only a few in lower; gums showed marked pyorrhœa in lower jaw, but no blue line.

The chest was emphysematous in type, and the respirations were markedly labored. The heart's apex beat was displaced outward; the impulse was short and weak. The right border of cardiac dulness was about 1 c.m. beyond the right sternal edge and the left 1 c.m. to left of the midclavicular line. The upper border was on a level with the third rib. Auscultation revealed a feeble first sound, a soft systolic whiff at apex, with slight accentuation of second pulmonary sound (relative insufficiency). There was some abdominal distention, but no ascites. Liver and spleen were slightly engorged.

On admission, the amount of urine was abnormally small, but after rest in bed, the use of saline laxatives and nitroglycerin, alternated with tincture of convallaria and digitalis, the urinary secretion increased to 64 ounces, while it again decreased during the last few days of life. The pulse was rapid, and toward the close of life compressible, while the respirations ranged abnormally high, particularly during the last four days. The temperature, which had been constantly at a subnormal level until four days prior to death, also became decidedly elevated, touching 104.6° at the time of demise. The physical signs of bronchopneumonia were present during the same period. Repeated urine analyses gave the presence of a heavy ring of albumin and numerous broad granular casts on microscopic examination; specific gravity, 1015 to 1019. The blood pressure in the recumbent posture was, systolic 168, and diastolic 138 mm. Hg.; during his stay in the hospital the blood pressure, however, declined considerably.

The ophthalmoscopic examination, made by Dr. L. Webster Fox, gave this result: Media clear; optic neuritis with marked œdema of the retina, extending back to the equator. The heads of the optic nerves completely buried, and outlines of arteries and veins quite obscured. Striæ of hemorrhages extending completely around the optic nerve entrances; apex of the swellings at least

nine to ten diopters in height. The ophthalmoscopic picture is that of a most pronounced case of albuminuric retinitis.

The patient was sleepless and decidedly breathless in paroxysms at night. Prior to the fatal termination, which occurred April 24, numerous subcrepitant and moist bubbling rales were audible over bases of the lungs.

The *autopsy* was made two and one-half hours after death. No rigor mortis; body still warm to the feel. *Lungs* œdematous; pleural adhesion on both sides (no free fluid); three small areas of

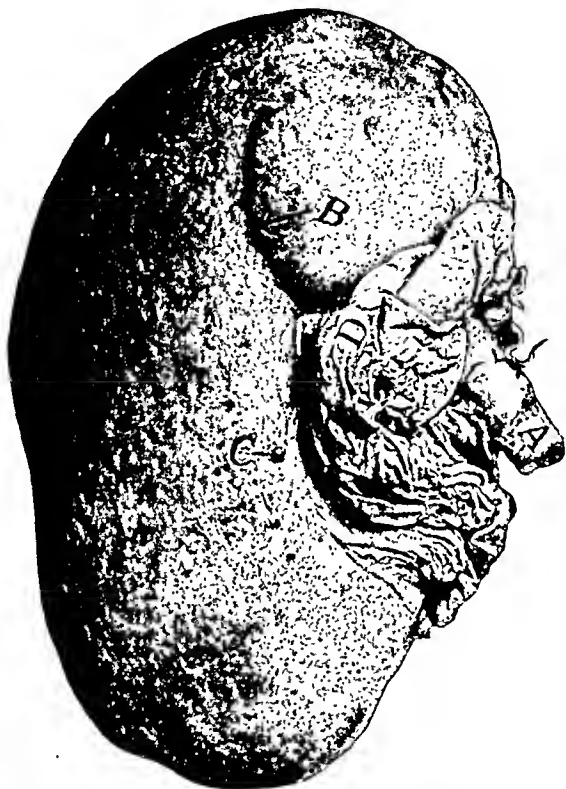


FIG. 1.—The kidney (reduced to three-fourths of its actual size). *A*, enlarged renal artery; *B*, attempt at lobulation; *C*, small retention cyst; *D*, reflected capsule.

consolidation were found—one in left apex, another in the lower lobe of left lung, and still another in the middle lobe of the right lung. These presented the characteristic appearances observed in bronchopneumonia. *Heart* showed general hypertrophy, with considerable secondary dilatation (relative incompetence); weight, 515 grams; valves showed no pathological changes, except slight thickening of the mitral segments. The *liver* was slightly enlarged and cirrhotic; *gall-bladder* normal; *spleen*, apparently normal; *stomach* and *colon*, normal in size and position.

*Kidneys.* The left kidney, renal artery and vein, as well as ureter, were entirely absent; also the left suprarenal body and

artery could not be found. The right or existing suprarenal body was somewhat hypertrophied. It was observed that the right renal artery was somewhat enlarged, and bifurcated just before entering the existing kidney. The remaining kidney (Figs. 1 and 2) was present in the normal position and much enlarged, weighing 240 grams (8 ounces); it presented a somewhat lobulated appearance. Macroscopically, it showed evidence of interstitial nephritis. The ureter on the right side, was also slightly increased in diameter, and on tracing it downward was found to enter the bladder in the normal

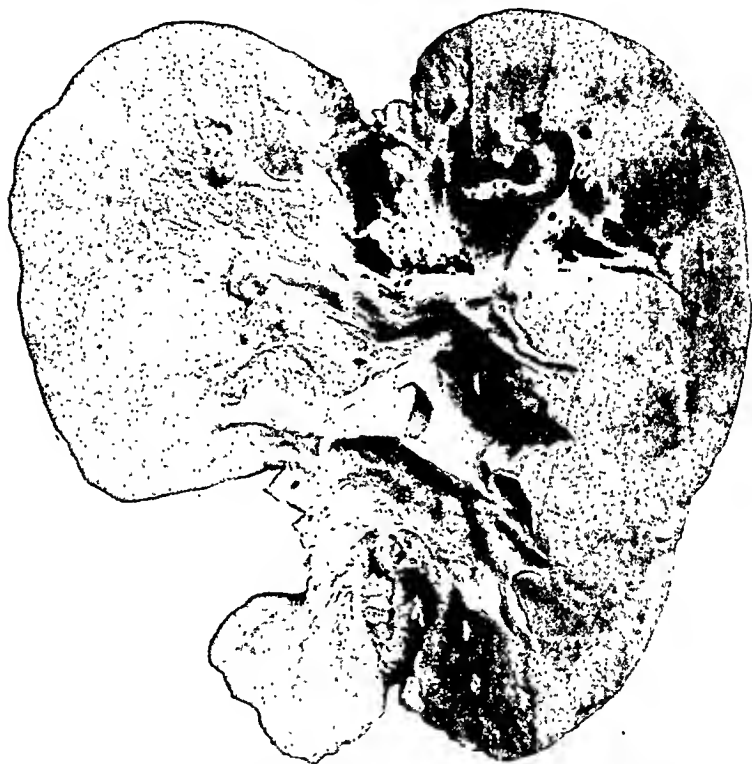


FIG. 2.—Longitudinal section of the kidney, showing a thick, somewhat irregular cortex and absence of the section removed for microscopic study (reduced to three-fourths of actual size).

situation. On the opposite side no indication of ureteral orifice was noted. The pelvis of the existing kidney, while proportionately increased in size, did not show the faintest evidence of an attempt at duplication. The genitalia on the side of the absent kidney showed nothing abnormal. The prostate gland was not investigated.

Dr. E. A. Case, the pathologist, reports on the existing kidney as follows: *Macroscopically*, the capsule strips with some difficulty, leaving a granular surface, with one retention cyst, about 3 mm. in diameter. The cortex is not thinned, as in typical interstitial nephritis, but as the man only had one kidney, this fact, and also the

massive size of the organ, are probably thus explained. The cortex is only a bit irregular in thickness. *Microscopically*, the glomeruli show varying changes. Some are larger than normal, with no pathological lesion save a congestion of the capillaries of the tuft. Others are shrunken; still others converted into hyaline masses surrounded by connective tissue. In some the Malpighian tuft has shrunken, leaving an appreciable space in Bowman's capsule. In some of the capsules of Bowman granular debris is to be seen, while others show marked thickening, due to the proliferation of connective tissue about them. The convoluted tubules show parenchymatous degeneration. The epithelial cells are swollen, very granular, outline between them indistinct, and the nucleus stains poorly. In the lumen of the tubules there is considerable granular material. The straight collecting tubules show less parenchymatous change, and many closely approximate the normal. The interstitial connective tissue is markedly increased, being especially marked about the glomerules, but also evident about the tubules. There is also thickening of the arterial walls. In the interstitial tissue of the cortex there is an irregular round-cell infiltration composed of mononuclear cells. The bloodvessels are congested, especially in the region of the collecting tubules and pyramids of Ferrein. It is evident that the material increase in size of the kidney is due principally to a numerical increase of certain anatomical elements. The pathological diagnosis is chronic interstitial nephritis, associated with which is a parenchymatous degeneration.

While this case was not a typical example of urogenital agenesis, it was a true instance of "single kidney," or unilateral urinary aplasia, with total absence of the suprarenal capsule on the same side—a rare and interesting anomaly. It is to be noted, therefore, that it does not lend itself to the investigation of the question of the relation of "single kidney" to anomalies of the sexual organs. On the other hand, the case furnished material for a further study of the compensatory enlargement of, and of the various lesions presented by, the existing organ.

Of my own tabulated list of 61 cases, 38 were males, 16 females, and in 7 the sex was not mentioned. The right kidney was missing in 29 cases, the left in 29, and in 3 the particular side was not stated. Of the 38 males, the condition occurred on the left side in 20, and right side in 18. Of the 16 females, the left side showed renal aplasia in 8 cases and the right in 7, while in 1 the side involved was not mentioned. Ballowitz found the condition on the left side oftener than on the right in the male, the ratio being 70 to 42, while according to my figures the proportion was about even, or 20 to 18. In the female, both sides are about equally affected, according to my figures (vide supra).

The ureter of the side of the congenital aplasia was absent in 42, present to a greater or less extent in 9, and in the remaining 10 no

mention was made. In 8 cases the genitalia were normal, in 19 abnormal, and in 34 instances their condition was not described. Of the 19 in which the genitalia showed hypoplasia, 11 were met with in the male and 7 in the female, while in 1 the sex was not stated. The precise character of the defects are briefly described in the tabulated list of cases, and it will be observed that they are remarkably variable, both as to degree and nature.

The suprarenal gland could not be found in 11 instances, was present in 26, and not referred to in 24. It was missing seven times in the male and four times in the female; or, in other words, in nearly even proportion in comparison to the totals for the two sexes. The renal artery was reported absent in 24 cases, present in 3, and unmentioned in 34.

The number of cases showing renal changes in the remaining organ other than mere hypertrophy was 27, those showing only hypertrophy, 7, while the renal changes were not described in 27. There were 15 cases, or 55 per cent. of the total number in which the lesions presented by the kidneys were described, that showed chronic nephritis, of which 8 were of the chronic interstitial variety. The findings in 3 cases were those of chronic parenchymatous nephritis, while 1 case presented the lesions of acute nephritis. Two patients showed tuberculous lesions, and 2 pyonephrosis; 3 had died of chronic diabetes mellitus. A single instance was furnished by each of the following conditions: Hydronephrosis, "abscessed kidney," calculus (ureteral), cystic kidney, congested kidney, amyloid kidney, and fatty kidney.

A similar consideration and analysis of all of the reported cases of solitary kidney in which the points at issue are detailed, or 286, gives us somewhat different and also more important generalizations.

*Sex.* In 248 cases the sex was mentioned, of which 159 were males and 89 females. As stated by Ballowitz, it is to be recollected that autopsies are less commonly made in the latter than in the former sex.

*Age.* Of 154 cases in which the age at death was given, 34 patients were under ten years; this number, however, includes 13 premature births. Between the tenth and fiftieth years 62 cases occurred, and after the fiftieth year 58 cases. Included in my series there was 1 case which had reached eighty-eight years of age, and another eighty years. These figures would indicate that longevity is not markedly abridged by the occurrence of this condition.

*Side.* Out of 286 cases, the condition occurred on the left side in 153, and on the right side in 120, with 13 not differentiated. In 158 males the congenital urinary aplasia occurred ninety-six times on the left side and sixty-two on the right. Per contra, of 83 cases occurring in the female, the left kidney was missing in 40, and the right in 43. It would appear, therefore, that the proportions for

the two sexes are diametrically opposed, but I am not in a position to offer a satisfactory explanation for the differences in sexual influence upon the side involved.

Out of the whole number, or 286 cases, the ureter was completely absent in 248. In 24 instances a more or less rudimentary ureter was in evidence, without the slightest indication of the presence of renal structure.

The presence or absence of the suprarenal gland was noted in 151 cases; it was present in 109 cases and absent in 42, or 27.8 per cent. In 14 cases the suprarenal gland on the side of the absent kidney was enlarged; in 2 it was atrophied. It is interesting to note that the suprarenal gland on the side of the existing kidney is rarely enlarged; for example, this was the case in 5 of the 61 cases included in my table, and in only 2 out of 111 cases tabulated by Ballowitz. In a single instance this organ was smaller than normal on the side of the remaining kidney. The condition of the genitalia was noted in 135 cases (out of the grand total, or 286), of which, 94 showed congenital defects, and 41 were obviously normal. Among the cases of genital hypoplasia were 40 males and 49 females, with 5 sexually undifferentiated.

It was found that 79 cases out of the grand total, or 170, in which the renal changes were given, or 46.5 per cent., showed morbid lesions other than mere compensatory hypertrophy. Among these 79 cases were: Chronic interstitial nephritis, 19; chronic nephritis (variety not specified), 11; chronic parenchymatous nephritis, 2; ureteral calculi, 9; pelvic calculi, 6; pyelonephritis, 10; cystic kidney, 3; tuberculosis, 2; hydronephrosis, 4; "diseased" kidney, 3; stone in the bladder, 1; carcinoma of kidney, 1; "cloudy swelling," 1; congested kidney, 1; amyloid kidney, 1; fatty kidney, 1; and abscess of kidney, 1.

Ballowitz speaks of the frequent occurrence of nephrolithiasis being emphasized by the older writers, and Mosler<sup>66</sup> refers to the danger to the individual attending disease processes affecting single kidney. The results of the combined statistics of Ballowitz, Moore, and my own indicate clearly that a greater than the normal percentage among subjects of congenital single kidney die of kidney complaints, as will be shown hereafter. Unquestionably nephrolithiasis is attended with peculiar danger to life in cases of single kidney in which the stone occludes the ureter. Obviously an effort should be made to remove promptly the calculus when single kidney is known to exist, after locating it by means of radiography. Indeed, the condition calls for unusual promptness if it is expected to save life. Obstruction of the ureter by a calculus has occurred after nephrectomy, and has been relieved by timely nephrotomy. Complete occlusion of a single ureter tends to the development of uremia, ending in death. The operation should be done at the end of forty-eight hours if spontaneous relief is not afforded.

Says Ransohoff,<sup>67</sup> there are records of eleven operations of solitary kidney—four nephrotomies and seven nephrectomies. The nephrectomies were fatal in from one to eleven days. The patient of Polk<sup>68</sup> lived eleven days. Traumatic rupture of a solitary organ caused death (as was to be expected) in a case reported by Taylor.<sup>69</sup> It is important to recollect that the ureteral orifice is generally absent on the side of the missing kidney. It follows that under these circumstances the condition under consideration is demonstrable by means of a cystoscopic examination; this should be, however, supplemented by catheterization of the ureters in cases in which two ureteral orifices exist, since in a small percentage of the cases of congenital single kidney a rudimentary ureter is present, extending upward from the bladder for a variable distance. It is highly probable that in a certain proportion of the latter instances, at least, the catheter could be introduced into the ureter for a short distance, but, obviously, not any urine could be segregated.

The importance of single kidney from a surgical standpoint can scarcely be overemphasized. The subject is also of special interest to the pathologist and internist, as shown by the fact that the advanced lesions of chronic nephritis were found in 32 of the fatal cases, or 42.3 per cent. Finally, it cannot be doubted that the development of either acute or chronic nephritis in cases in which renal agenesis exists gives a less hopeful outlook than when these arise under normal conditions, that is, bilaterally.

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THE TREATMENT OF RHEUMATIC FEVER.<sup>1</sup>

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**THEORIES OF RHEUMATISM.** It is not my purpose to discuss the numerous theories advanced to account for the phenomena of acute rheumatic fever. I will merely state that it is the consensus of opinion at the present time that the disease is an acute infection. Numerous observers have claimed to have isolated the specific organism, among the most insistent of whom are Poynton and Payne. To the former has been lent the weight of the authority of Osler's new *Modern Medicine*, to the pages of which he contributes the article on rheumatism, and in which the various views of the etiology of this disorder are set forth in some detail.

**AGE.** About one-half of all cases of rheumatism occur between the ages of fifteen and twenty-five years; about one-quarter in the next decade, that is, between twenty-five and thirty-five years. My own impression, based on considerable contact with children, is that the figures set for childhood are too low, as the disease is peculiarly insidious at this age, and deviates strikingly from the type as established in the adult. The serious complications are quite as common, even more common than in the adult. Of the cases occurring in childhood, 70 per cent. fall between the ages of ten and fifteen years.

I cannot refrain from intercalating a bit of pediatric wisdom at this juncture: (1) Beware of a diagnosis of rheumatism in infancy. It is so rare that, when authentic, it warrants rushing into print, which is saying a good deal. The so-called rheumatic joints of infancy are almost certainly pyogenic, scorbutic, or syphilitic. (2) Scan every child's heart with care, and seek constantly in the histories for tonsillitis, stiff neck, and especially "growing pains." How many children's lives have been sacrificed to that unfortunate term no man can estimate.

**SYMPTOMATOLOGY.** That the disease is rather abrupt in its onset, accompanied by fever, that sore throat is not uncommon, that drenching acid sweats may occur, and that the inflamed joints are the pathognomonic sign, is all well known, and is reiterated here merely to emphasize the points of attacks in the application of therapy. The complications are the important events in the course of rheumatism, and will be considered after rules have been laid down for the simple, uncomplicated case.

<sup>1</sup> A lecture delivered at the Cornell University Medical College, New York.

**THERAPY.** A sick man invites medical attention for two reasons: First, he wants to be cured of his disease; and second, he wants to be made more comfortable during his illness. To treat a patient intelligently, it goes without saying that a diagnosis is imperative, but the intellectual satisfaction derived from establishing a diagnosis must not lead to a satiety that eschews further effort directed toward relief of the condition. Such a comment is justified by fact. Still another function to be subserved by the physician is the instruction of the patient how to avoid a repetition of the attack. There are certain measures that may be directed toward any acute illness, others that are aimed at the particular disease in question. This order will be preserved.

*Rest.* In the rheumatism of adults the painful condition of the joints impels rest, willy-nilly, but this by no means obtains in children. Pain, which he who suffers it looks upon as an unmixed evil, is more often a boon than a bane. If one will get in the habit of analyzing the symptoms of disease in terms of efforts on the part of Nature to accomplish a useful purpose, or as expressions of compensations, he will be amazed to see how many hints these symptoms give that they are to be utilized as allies, not combated as enemies.

In rheumatism there are three emphatic reasons why rest should be insisted on: (1) Because the body cells are busied in combating an intoxication, for which their energy should be conserved as much as possible; (2) because certain tissues are undergoing the alteration incident upon inflammation, and are struggling to accomplish repair; and (3) because the spectre of cardiac involvement is never absent from the disease, and we fear that every increment of activity on the part of that organ may heighten the possibility of the dreaded disaster.

To illustrate the significance of rest, I will cite the following figures: One knows, as a fundamental physiological fact, that the energy and heat of the body are derived from the combustion of the foodstuffs, and that the carbon of these foodstuffs is in large measure eliminated from the body through the lungs as  $\text{CO}_2$ ; so we can collect and estimate the amount of  $\text{CO}_2$  eliminated in a unit of time, and look upon the results as expressions of the activity of the body cells during that period. This has been done repeatedly, and the same individual who during sleep eliminates 22 grams of  $\text{CO}_2$  per hour will, when awake and exercising the greatest amount of muscular relaxation possible, eliminate 31 grams, and under conditions ordinarily considered those of rest, 38 grams. In this light, rest assumes a meaning, and the importance of restlessness and loss of sleep in disease is enhanced in dignity.

The two important factors to be considered in estimating the amount of work done by the heart are the amount of blood expelled and the pressure, that is, resistance, to be overcome. The lessened

heart rate in recumbency and the diminution, even though moderate, of blood pressure in this attitude will suffice to emphasize the importance of rest to this organ.

Rest should be in bed. One might suppose this injunction to be superfluous, and yet it is everyone's experience not infrequently to find himself in the presence of contentious individuals who demand many reasons, when it might be supposed common sense would dictate; and one might as well write in golden letters on the tablets of his memory that he is to treat individuals, whose very individuality depends on differences, not machines nor yet diseases.

*Bed.* The bed should be of a height and width most convenient for handling the patient, who is in many instances helpless, and to whom the most gentle handling may constitute torture. A half, or at the most three-quarter bed, with a woven wire spring, sufficiently stiff to prevent sagging, should be chosen. The standard hospital bed is an admirable example. The mattress should be soft, but resilient and firm. A good hair mattress is preferable. If the patient perspires freely, the bed should be made with thin blankets instead of sheets. The patient should wear a thin flannel nightgown, opened all the way down the front and slit along the sleeves, so that the joints may be exposed for inspection or treatment with the least disturbance, and it is well to throw a thin flannel cape about the shoulders. The nurse should be instructed to put the clothes on this bed with a view to the comfort of the patient, rather than to preserve the symmetrical and esthetic effect so often insisted on in the hospital ward, regardless of the comfort of the patient. Often the lightest touch of the clothes is agonizing to the patient, and hoops, cradles, or other contrivances to take the weight of the clothes off the patient must be utilized.

*Room.* The best available room should be chosen, with a view to an abundance of light and air, with a southern exposure in the winter, and away from the prevailing winds at all times. The bed should be so placed that the draughts may be avoided but the air not shunned. The therapeutics of light is not duly appreciated. The minds and bodies of many of us are as responsive to its influence as a photographic plate. I hope on another occasion to go more into detail about this matter. Air should be admitted to the room freely. There can be no superfluity of fresh air. In summer the windows should be kept wide open. In the winter the room should be frequently aired and kept at 65° to 70° F. Personally, I do not hesitate to admit the cold clear air of a winter's day to the sick room, observing proper precautions with reference to the patient's coverings.

*Diet.* If there is any one field within the province of medicine that promises richer yield than another for the labor expended on it, it is that of dietetics. As yet it is almost virgin, and still such results as have been obtained are of the highest significance. It

has been well suggested that if the physician would give the same amount of time, work, and care to the prescription of foods that he does to drugs, enormous benefit would accrue to his patients.

In the first place, a sick man needs food, and he needs more food than is ordinarily given him. Of course, one grants that there are certain conditions that make the administration of sufficient food difficult or impossible, but that does not obtain in the majority of instances. As I have said, the energy and heat of the body are derived from the combustion of its foodstuffs, and as energy can be converted into heat, the value of the foodstuffs can be expressed in heat units. Moreover, the amount of energy and heat the body gives off in a day can be measured in terms of heat units; so that we can determine just how much food an individual of a given weight, under varying conditions of activity, needs. The term adopted to express a heat unit is the "calorie." The amount of heat that 1 calorie represents is that required to raise 1 kilogram of water from 0° to 1° C. This calorie is sometimes spoken of as the "large calorie." The "small calorie" is the amount of heat needed to raise 1 gram of water through 1° of heat; therefore, 1 "large calorie" equals 1000 "small calories." Unless qualified, the term "calorie" means a "large calorie."

Now, under what is ordinarily known as rest, a man gives off heat in twenty-four hours equivalent to about 33 calories per kilo of body weight; that is, a man weighing 70 kilos, or 154 pounds, will give off about 2300 calories. This amount of heat must be replaced by his foodstuffs to keep him in equilibrium.

The patient with rheumatism, however, is suffering from fever, and in fever he gives off not only what he does in health at rest, but some 20 to 30 per cent. more. If we add 25 per cent. more to our estimated calories at rest, we find the patient's needs are 2800 to 2900 calories. We are all aware that in febrile conditions it is customary to put a patient on a milk diet, because the different food constituents—fat, carbohydrates, and proteids—are so well represented in it, because it is bland, and because it is easily administered. The physician's instructions frequently are a glass of milk every two hours. A glass is supposed to hold 8 ounces; more commonly, as given, it holds 6 ounces. On this schedule, ten feedings would be exceptional, and eight nearer the actual number; so the patient would get  $1\frac{1}{2}$  to 2 quarts of milk a day. In a quart of milk there are 620 calories of food; in the patient's dietary, 930 to 1240 calories, or one-third to two-fifths of his needs as calculated. But the case is even worse than this, for, as I shall later show, there are reasons why, in fever, a patient's dietary needs are greater than those set out above.

It is an easy mathematical problem to determine that to meet the patient's needs with milk would require some 5 quarts of milk, and the administration of over a gallon of milk day after day does not

appeal to our common sense. To keep within quantitative limits, qualitative changes must be made in the food. The readiest way to do this is to add to milk, cream to furnish more fat, or starch, or sugar, to furnish more carbohydrates. For example, enough milk sugar can be added to the milk to make 10 per cent. without making it disagreeably sweet; or cereals, to make gruels or milk soups. Six per cent. of sugar added to milk will give a milk equal to about 860 calories to the quart.

In addition to milk, cereals, bread and butter, rice, and cereal or milk soups are permissible. An ordinary thick slice of white bread ( $1\frac{1}{2}$  ounces) furnishes 100 calories; an average pat or ball of butter (a little less than  $\frac{1}{2}$  ounce) the same; an ordinary helping of boiled rice (4 ounces) as much more, and  $1\frac{1}{2}$  ounces of cream the same. Even 3 teaspoonfuls of granulated sugar affords 100 calories. There are 100 calories in a large serving of oatmeal or hominy.

This necessity for a sufficient diet obtains especially in long-continued fevers, while in the brief fevers of intense character, in which the functions of the digestive organs are impaired, only small amounts of food are to be urged, as the body has a surplus to meet its needs for a short time.

I have introduced these figures thus early to concentrate attention on a branch of our art that has been left too little cultivated and exercised without reason. Milk, milk soups, cereals, bread, and rice form the staple diet in rheumatism. To meat soups, which have scarcely any nutritive value, there are certain theoretical objections, but if their well-known influence in spurring a jaded appetite and stimulating what the Germans call the "appetit-saft," is taken into consideration, I think their administration in small amounts is warranted. With the decrease in the fever, eggs may be used, and in convalescence, fish, meats, and vegetables.

*Bowels.* When called to attend a patient suffering from an acute infectious process, it is a good rule to assure satisfactory evacuation of the bowels. Just how much additional disturbance a neglect of this measure may induce we do not know, but we are aware of the fact that at times in an individual otherwise well, constipation may incite symptoms akin to acute intoxication, or more commonly, depression, malaise, anorexia, and headache, and we have evidence that products of decomposition in the bowel, normally absorbed and paired, like the indol group, with sulphuric acid, can, when this function of pairing is interfered with in disease, give rise to toxic manifestations.

An active saline, like magnesium sulphate or Epsom salts, sodium sulphate or Glauber's salts, or sodium potassium tartrate or Rochelle salts, in doses of 1 ounce, or, in patients susceptible to saline purgatives,  $\frac{1}{2}$  ounce, may be given, assisted by a soapsuds enema four to six hours later, if the salts have not been sufficiently effectual.

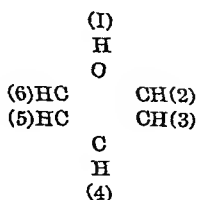
It should be remembreed that the feces represent an excretion

from the bowel of mucus and other substances which represent nitrogenous metabolism, and afford a pretty constant percentage of the total nitrogenous output; that the feces are not mere food residues, and, in fact, normal feces should contain but very little food residue other than indigestible fibers of cellulose, seeds, etc. Hence it is surprising to the patient, and often to the physician, too, to discover so large results from catharsis when the patient has been on a milk diet, or even when on no diet at all. With this knowledge, then, of the formation of feces with a low or easily digestible diet, the necessity of attending to periodical evacuation is emphasized. This may best be done by enemata in most febrile diseases, but with the discomfort incident upon handling any of the body in rheumatism, further doses of salines may be preferred. I believe that too frequent catharsis by drugs entails an irritation that in itself may become mischievous.

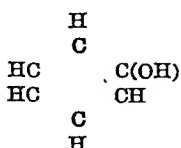
*Specific Treatment.* It was once hoped that every disease might be met by a specific drug, and it was once believed that many diseases were cured by specific drugs; but as medicine entered on an era of more searching observation, and had to rest its judgment on scientific criteria, the number of specifics dwindled, until specific treatment has come to connote the treatment of one disease alone.

When Dr. MacLagan, of Edinburgh, in 1874, began to use salicin, a glucoside of salicylic acid obtained from the young bark of the willow, in rheumatism, which was quickly followed by the introduction of other forms of salicylic acid, the change that came over the clinical picture of this disease, that turned a bed of racking pain into a couch of relative comfort in a few hours, and a patient to whom the least touch was agonizing into one who could be handled with relative impunity, warranted the belief that a specific had, indeed, been discovered. It is said that we no longer see rheumatism as it was presented to the older practitioners, and yet the drug can not be called specific, if we mean by that one that can eradicate the disease. That its discovery was a boon, no one who has witnessed its effects can for a moment doubt.

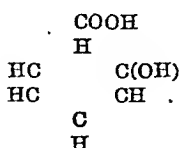
Salicylic acid has this structure:



is the benzene ring. If you will replace the H at (2) by an -OH group, that is, make an alcohol of it, you will convert it into a well-known poison, carbolic acid.



Note what slight changes in a complex group and the introduction of what simple radicles induce potent changes in character. We have but to make another slight change, by introducing an acid radicle at (I), to convert the toxic carbolic acid (which is no acid at all, but an alcohol) into the substance in question, salicylic acid.<sup>2</sup>



I might add that the introduction of an acid radicle into the structure of a toxic alcohol detoxicates it. This is a general law.

This substance is classed among the antipyretics and antiseptics; it is also an anodyne. Its therapeutic value is exercised in all three directions in rheumatism. Salicylic acid may be administered as such, or in the form of a salt or ester. The effect is the same in kind in all these forms, but certain by-effects determine the use of one or the other. It should be administered in full dose. Its failure may often be attributed to insufficient dosage. Its toxicity is slight. In an adult of average weight I give as much as 20 grains of one or the other form of the drug every two hours for the first twenty-four hours during the waking period, or even for forty-eight hours. In severe cases even 30 grains may be given for the first two or three doses. When the pain subsides the dose may be cut down gradually to 15, to 10, to 5 grains at a dose, how much and how rapidly depending on the progress of events or on signs of accumulation. The dose should be well maintained at amounts of 10 grains every two hours until the active phases, as evidenced by fever, pain, and joint swelling, have passed. Just how this drug acts in rheumatism we do not know, but its effects are so much more prompt and satisfactory in this condition than in any other clinically akin to it, that we are impelled to believe that it has some effect on the materies morbi directly; so that it is my custom to keep the patients on considerable doses—5 to 10 grains every two or three hours for a week or ten days after the subsidence of acute symptoms, and for four to six weeks on lesser doses of 5 grains three or four times a day, administering the drug much as we do quinine in malaria.

<sup>2</sup> Salicylic acid is not derived in this manner, but from ortho-oxy-benzyl alcohol  $\text{HO.C}_6\text{H}_4\text{CH}_2\text{OH}$ . The illustration is used to draw attention to the chemical kinship of well-known drugs which are so different in their action.

Disagreeable symptoms sometimes ensue; more often disagreeable than dangerous. They are: (1) buzzing, roaring in the ears, with varying degrees of deafness; (2) gastric disturbances; (3) cardiac disturbances; (4) respiratory disturbances; (5) cerebral symptoms; (6) renal complications; (7) hemorrhages; and (8) skin involvement. This looks like a formidable array of disasters, and so do tidal waves, cataclysms, and the fall of meteors in the catalogue of everyday possibilities; but, like most apparitions, this list takes less substantial proportion when submitted to light. I will consider them in the reverse order. Skin eruptions after the use of the salicylates are rare; still a diffuse erythema, an urticaria, a hemorrhagic outbreak, and other forms may follow. It will be observed that the three forms specified have all been associated with rheumatism, and it would be difficult to determine in all cases the association of the drug with the rash. They are not dangerous in themselves, and the drug should not be intermitted on their appearance unless clearly aggravated by the continuance of the drug.

Retinal hemorrhages are still more uncommon, while epistaxis has been more frequently reported, and, if severe, might enforce cessation of the drug. Albuminuria and hematuria, which have been attributed to the irritating effects of salicylates, may be caused by the disease itself, but with their appearance it might be wise to intermit the treatment until it is demonstrated that they do or do not play a part in the disturbance. There can be no doubt that now and then the salicylates have induced an active delirium, sometimes like an acute mania. I recall a report of two such cases occurring at Bellevue Hospital, but it is very unusual. It must not be forgotten that delirium intervenes in the course of rheumatism, especially, it is said, with the onset of a pericardial involvement, and associated with hyperpyrexia. Dyspnoea, characterized by slow and labored breathing, has occurred, and suggests the possibility of impurities in the drug, as, indeed, does the slow heart and threatened collapse occasionally noted. Here, too, one must keep in mind the involvement of the myocardium in the disease. However, in either instance, so threatening a condition should indicate a withdrawal of the drug.

To sum up, I should say that the above-mentioned conditions are rare; that they may be attributable in some instances to the disease rather than to the drug, in other cases to impurities in the product used, and finally, to idiosyncrasies—that peculiar reaction of the individual to drugs, food, and environment that takes him out of his class and constitutes in him an anomaly, and defies foreknowledge. I firmly believe that it is only a minority of the above-mentioned conditions that can be attributed to the drug itself.

It stands otherwise with the first two disturbances enumerated. They are to be attributed to the drug, and their occurrence modifies



our action. The ringing in the ears and a mild grade of deafness may be looked upon as a limit of tolerance with comfort rather than a menace. There is no reason to intermit the drug on this account, but if the discomfort is considerable, the dosage should be cut down. The gastric irritation resulting upon the administration of salicylates is the *bête noir* of the practitioner. It is for this reason rather than for any other that so many forms of salicylates are in use. There are certain forms of the drug from which one may anticipate more irritation than from another, but, again, the susceptibility of a particular stomach to a particular preparation cannot be predicted with any degree of assurance.

I advise, as a rule, the use of the preparation that has stood best the test of time and experience. In this case it is the sodium salt of the acid. I may say at once that the acid itself is too irritating to administer internally over a length of time. Order the drug alone, in simple solution. Do not fall victims to polypharmacy. Good polypharmacy is an art that few attain, if, indeed, it is attainable. The polypharmacy that most of us practise label us as copyists. Be sure that the drug is chemically pure. There are two ways of attaining a pure drug: First, specify the chemist's, that is, manufacturer's name; second, send the patient to a druggist whose honesty is his commercial success. Unless this precaution is taken a cheap synthetic sodium salicylate, contaminated with the by-products of its synthesis, may be used, and to these impurities may be attributed much of the gastric irritation and other toxic manifestations of the drug. Order the dose to be taken well diluted.

For example, write thus:

R—Sodii salicylatis . . . . .	15.0
Aque destillatæ . . . . .	q.s. ad 60.0
M. et S.—One teaspoonful in water every two hours.	

One will note that this calls for a 2-ounce mixture, but is written in the metric system, and that there are just as many grams in this 2-ounce, or 60 c.c., mixture as I want to give grains in one dose. Even the water has as many cubic centimeters as I want to give drops in a dose—60, that is, 1 teaspoonful.

Sometimes the salt is better borne and less disagreeable to the taste if a little glycerin is used, as:

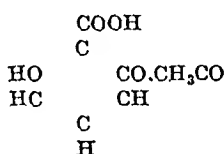
R—Sodii salicylatis . . . . .	15.0
Glycerini . . . . .	15.0
Aque destillatæ . . . . .	q.s. ad 6.00
M. et S.—One teaspoonful in water every two hours.	

If one has doubts about his patient's ability to get a good salt, he should order the salt made fresh from salicylic acid by adding sodium bicarbonate. This is a very excellent way of writing the prescription:

R <sub>y</sub> —Acidi salicylici . . . . .	15.0
Sodii bicarbonatis . . . . .	q.s.
Aquæ destillatæ . . . . .	q.s. ad 60.0

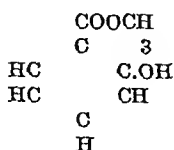
M. et S.—One teaspoonful in water every two hours.

The druggist is to use of the soda what is needed; he adds definite proportions of the two drugs, if he follows the Pharmacopœia, or he simply adds soda to the solution of the acid until effervescence ceases, that is, until no acid is left to liberate the CO<sub>2</sub> from the soda. If, for any reason, sodium salicylate is not well borne, one may have recourse to another form of the drug. My own preference is for aspirin, which is an acetylsalicylic acid; that is, it is salicylic acid in which the H of the OH group has been replaced by an acetic acid radicle, CH<sub>3</sub>CO; thus:



This substance is a white powder, formed of small crystalline needles, practically insoluble in water (100 parts) and in acids, so that it passes through the stomach for the most part unchanged, and is broken up in the intestine. It is less irritating to the stomach, but that it should be devoid of all the disadvantages of the sodium salt its chemical structure forbids us to believe. I have in one instance seen a massive angioneurotic œdema of the face follow a single small dose, and have seen three such cases reported in the literature since. However, I believe it to be a very valuable form of salicylic acid. It is best prescribed in capsules. The dose is practically the same as the sodium salt, or about 15 grains for a beginning dose.

Another excellent preparation of the salicylic acid series is the ester, methyl salicylate, that is, salicylic acid in which the H of the acid group is replaced by methyl CH<sub>3</sub>; thus:

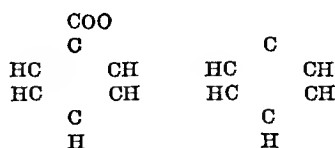


Methyl salicylate is a volatile oil that constitutes well over 90 per cent. of the oil of wintergreen, the well-known gaultheria procumbens of our woods, and of the oil of birch, oleum betulæ, obtained from the bark of the sweet birch, betula lenta, or is produced synthetically, and when carefully prepared should answer the purposes of the natural oils. Of the three, the oil of wintergreen is, as a rule,

preferred. It may be given in capsules, in emulsion, or in milk. I very much prefer the capsules, because in emulsion the decided taste of the drug, which may be agreeable at first, soon palls on the patient.

As for its administration in milk, the same objection obtains, and what is much more important, it violates a rule that I believe one should invariably observe—never give medicine in food, for, if the medicine does disagree, its association in the mind of the patient with the food may produce a disgust for food which may be the mainstay of the case. The drug is usually very well borne, but its decided taste, even when given in capsules, for the slight eructations it often induces is a constant reminder, is the chief drawback. One will rarely have to choose outside of one of these three forms of salicylic acid in the treatment of rheumatism. If he does, the great probability is that he has not administered these forms properly, or that the patient cannot stand salicylic acid in any form, or that the series does not meet the needs of this particular case.

I will mention two other well-known preparations: First, the original drug, salicin. This is a glucoside, which can be split up by acids into grape sugar and saligenin, the active principle, which is the alcohol from which salicylic acid is formed, and this formation of the acid goes on in the body after its administration. It is a white powder, bitter to the taste, rather insoluble in water (28 parts), so best administered in capsules. It is well borne, and by many preferred for children. The dose is the same as for the others. Second, salol, another ester, phenylsalicylate, that is, salicylic acid in which the H of the acid group is replaced by phenyl  $C_6H_5$ ; thus:



It is a white powder, almost tasteless, and quite insoluble in water. It passes through the stomach for the most part unchanged, and is broken up in the intestine, two-thirds of it appearing as salicylic acid and one-third as carbolic acid. It is administered best in capsules or powders, or can be suspended in mucilage of acacia. It has no advantage over the other forms in rheumatism, and has the disadvantage of affording only two-thirds of its weight as the desired substance, while one-third is the toxic carbolic acid, which can produce its characteristic poisonous symptoms when given in large doses. The dose is about the same as for the other preparations.

As I have already intimated, some patients cannot take salicylic acid in any form. We cannot, for that reason, neglect their need for

relief of pain. The three drugs in most common use for such a purpose are acetanilide (antifebrin), antipyrine, and phenacetin (officially acetphenetidinum). Of these three, the first is the most potent, also the most irritating and toxic. These drugs are not given over a long period, as the salicylates are, but as needed, to control pain. Often small doses, frequently repeated, are as efficacious as fewer large doses. Acetanilide may be given in doses of 1.5 grains every half hour for four doses, or 2 to 3 grains every two hours. If there are heart complications, it should not be used. Phenacetin may be used in twice the dose. The dose of antipyrine lies between the two. These drugs should be promptly stopped if cyanosis appears, which is well before cardiac or respiratory failure threaten, and, of course, as soon as pain is relieved.

If the pain is severe, rather than push these coal tars to large doses, one should use morphine, in small doses, hypodermically,  $\frac{1}{16}$  to  $\frac{1}{8}$  grain. Morphine in any illness of length should be used reluctantly and in minimum dose, lest a habit be established. Two other drugs have been much used to control pain—potassium iodide and colchicum. Their bad effects on the stomach are too certain, and their beneficial effects on the condition too dubious, to encourage their use.

Another line of treatment, originated in England by Fuller to combat an acidity that at that time was looked upon as an etiological factor in the disease, is the "alkaline treatment." This treatment met with little favor elsewhere in Europe, but was adopted in this country to a considerable extent, and still has considerable vogue. By many men it is used when the salicylates are not well borne; by others when cardiac complications threaten or exist; and by a very great many in conjunction with the salicylate treatment. In my own opinion the treatment has been dictated more by tradition than by manifest evidences of its efficacy, as in the case of the salicylates, and yet I am not prepared dogmatically to negative the judgment of so many good observers. One should choose the milder alkalies—sodium bicarbonate, potassium citrate, or potassium acetate; for example, 20 grains of sodium bicarbonate every two hours until the urine reacts alkaline, and then every three hours, or in a little less dose, or enough to continue the urine alkaline. Those who are enthusiastic in its use claim that cardiac complications are less likely to ensue, or, if occurring, they are less severe.

**SYMPTOMATIC TREATMENT.** The symptoms that give character to this disease are those referable to the joints. The improvement in the local manifestations of the disorder under salicylates constitutes one of the most satisfactory evidences of their potency, and yet the resolution of these parts often lingers well behind the disappearance of the fever and the pain; and, moreover, much can be done during the height of the disturbance to ameliorate the discomfort, hasten the resolution, and prevent bad sequels.

*Rest.* For an inflamed joint, just as for a broken bone, rest is imperative. Pain, which I have said is Nature's agent, impels rest, but when pain is banished or mitigated under our ministrations, the patient uses the joint too early, and often to his great detriment. The position of the limb in semiflexion is one involuntarily chosen as the most comfortable, and may be preserved during the acuteness of the attack. Various devices are used to maintain a single position. We can bolster the limb by putting pillows under the knee or on either side, and find similar arrangements for the other joints. This, of course, can not assure a high degree of immobility, and we can secure better results with splints, well padded and carefully applied. The success of these devices depends on the care and skill with which they are applied, and if simply suggested by you and left to the devices of unskilled hands in the application will be far worse than useless. Still another way to attain the desired end is by applying stiff bandages of plaster-of-Paris or starch. Again, much care must be taken in the application, as the parts cannot be daily inspected, and rough folds in the bandage, bits of dried plaster next the skin, which is moist with the excessive perspiration, can induce sores of serious import. These casts must be reapplied as the effusion in the joint disappears. On the whole, a good splint is, I think, the best device.

*Heat and Cold.* The patient's testimony is sufficient evidence of the comfort these measures afford, whatever opinion may be entertained with reference to their curative qualities and the rationale of their action. From the standpoint of comfort the reaction of different patients to heat or to cold differs widely. To one patient, with a painful joint, cold gives almost instant relief, while in another the pain is intensified, and finds relief from heat, and vice versa. Continuous cold exercises considerable anesthetic effect, and may be secured by the application of the ice coil, or the more readily obtained and manipulated ice bag. Ice bags of various shapes may be obtained, but the circular ice bag does well for most purposes. The ice bag must be properly filled in order to make its application efficient. The ice should be cracked in pieces not larger than the end of one's thumb, and enough to cover the bottom of the bag. Enough cold water is poured on this to enable one to force all the air out of the bag and screw the cap down to the level of the water. This procedure leaves the bag supple, so that it may be wrapped around the part, which the presence of air makes impossible. Protect the part with a thin layer of vaseline or oil and a thin layer of cloth. A long-continued direct application of ice to the skin may do damage to that structure. Heat is best applied by fomentations. A couple of layers of flannel are wrung out of boiling water in a wringer made of a crash towel, and applied snugly to the joint. This is repeated three or four times, at intervals of ten to fifteen minutes. The parts are then sponged with water at about

75° F., and wrapped in flannel or non-absorbent cotton. A soothing application is the cold compress. This is done by wringing two or more layers of linen or old cotton cloth or cheesecloth out of water at about 60° F. and applying snugly to the part. This in turn is covered by dry flannel. These applications are renewed about once an hour. The effect of cold is momentary; the vessels soon dilating and conveying heat to the surface, warm the compress to the temperature of the part drying it. The reaction induces a hyperemia, the value of which will be touched on at some future time. The joints should at all times be well protected from changes of temperature. This is best done by wrapping them in layers of non-conducting material, like flannel or non-absorbent cotton or cotton batten. The number of drugs that have been used locally are legion. I will purposely refrain from mentioning more than one or two that I have found helpful. Perhaps the most common application is methyl salicylate. That it does any more than any other volatile oil, by inducing a hyperemia, I doubt. That the salicylates may be absorbed by the skin I have proved to my own satisfaction, but not in such amounts as to make that the object of the application. The methyl salicylates may be applied pure, or in the form of an ointment. The following is one in much use:

R—Methyl salicylatis,

Menthol . . . . .	5ā	15 per cent.
Petrolati . . . . .	q.s. ad	1 oz.

An ointment containing ichthyol has been much praised. For example:

R—Ichthyol . . . . .	25 per cent.
Petrolati . . . . .	q.s. ad 1 oz.

M. et S.—Local use.

*Counterirritation.* Counterirritation is a very old remedial measure, which has survived the rise and fall of countless therapeutic efforts, and the very persistency of which, in this Nihilistic age, speaks for its reality. It is indicated rather in the subacute or chronic stages of joint inflammation than in the acute. Of the many means of inducing it, I will mention two only as worthy consideration—the cauterization and the fly blister. Of the two, the former is much the better, as being easier of application, easier of control, less likely to be followed by bad results locally, and entailing no danger from absorption. The cauterization is flicked lightly over the part, care being taken to avoid severe blistering or deep burns. The part is then smeared with vaseline, oil, or ointment.

In applying the blister (*ceratum cantharidis*), it is cut about one inch square. In making the application to the knee, four such might be used, one above and one below on either side. Shave and cleanse the part. Oil the edges of the blister and apply a little

vaseline to the skin adjacent to the blister, to avoid its spreading. Leave the blister in position for four to six hours, and if a blister has not formed in the skin by this time apply a warm poultice to the part, which will hasten its formation. Puncture the blister on its dependent edge, evacuating the serum but not destroying the protecting epithelium. Dress with oil. Some of the disadvantages of the blister have just been set forth, and in the presence of a damaged kidney, as may occur in the course of rheumatism, the dangerous irritating effect of this drug on the parenchyma of the kidney, which it causes in the course of its excretion, must be kept in mind.

*Pressure.* When an effusion is slow to absorb, one may hasten the result at times by applying a snug bandage of flannel or rubber, which will exert a continuous but moderate pressure.

*Later Measures.* As the disease is prolonged, chronic changes in the joints threaten. Care must be exercised to prevent ankylosis. Splints must be occasionally removed and plasters and bandages taken off. Gentle manipulation of the joint must be carried out; or intelligent massage, hot fomentations, hot air baths, and baking had recourse to to facilitate absorption and resolution. In these later stages it is still believed that the iodide of potassium may do good.

*COMPLICATIONS. Hyperpyrexia.* The sudden onset of excessively high temperature, with extreme restlessness, headache, vomiting, delirium, and later coma, suggestive of meningitis, while occurring in the course of other febrile processes, is relatively common in rheumatism. It must be treated promptly and on the same principle as a sunstroke, that is, by a rapid withdrawal of heat. This is effectually done only by the use of cold baths or packs. The patient is put into a tub at 65° F., or, if the shock is too great, the water may be warmed to 80° F., and as the water warms from the patient's body heat, the temperature is kept down by adding ice to it. The patient should be kept in the bath until the temperature falls several degrees. If a fall to about 102° F. can be attained, the patient should be removed from the bath, as the temperature will often continue to fall. During the bath, ice or cold water should be applied to the head. The bath should be repeated as often as the temperature rises to between 104° and 105° F. If the patient becomes chilled, is cyanosed, the temperature falls well below normal, or collapse threatens, he should be removed from the bath, put in warm blankets, heat applied, and stimulants freely used. A cold pack, the wet sheet in which the patient is wrapped being continuously rubbed with pieces of ice until the desired drop is obtained, is sometimes quite as efficacious as the bath.

*Cardiac Complications.* The frequency of these complications, and their gravity, threatening not merely the patient's life in the present attack, but, worse yet, his future, dooming him to a life of invalidism and dependence, make them by far the most important features of the attack, and haunt the physician from the incipency

of the disease. A visit should never be completed without a careful examination of the heart. Changes in rate, rhythm, quality of sounds, or the appearance of adventitious sounds, should immediately put the physician on his guard. It cannot be too emphatically insisted that the mildest attack, as judged by fever, pain, joint implications, and general discomfort, may still be accompanied by grievous heart implication.

Statistics vary, but from reliable sources it is gathered that pericarditis occurs in 15 per cent. of the cases, and endocarditis in over 50 per cent.; in children under ten years, in as high as 75 to 80 per cent. It must be remembered that a more proper term for what actually exists in the heart is pancarditis, for the whole structure is likely to be implicated. The treatment of these conditions is the same as when occurring under other circumstances, and is dealt with elsewhere. The only question to be discussed at this juncture is the use of salicylates. Some authors fear the depressing effects of the drug. Others maintain that the condition responds more favorably to the alkaline treatment. Others still consider that the appearance of the cardiac complications indicates no change in the treatment. Personally, I have always continued the salicylates; but if, in addition to evidences of inflammation, the heart shows that it is becoming incompetent, I then stop the salicylates or any drug that may confuse a judgment of the factors concerned, and rely on the ordinary measures pursued in heart disease.

*Pulmonary Complications.* Pneumonia and pleurisy occur in a considerable number of the cases, some authors giving the figures as high as 10 per cent. I, myself, have seen it frequently in the severe rheumatism, and always with the cardiac involvement. The treatment is such as would be instituted under other circumstances.

*Other Complications.* Sore throat, urticaria, sleeplessness indicate no special considerations, as occurring in this particular disease. Anemia is a striking feature of the disease, and indicates in convalescence the use of iron and iron-containing foods. Sweats of a severe type have long been associated in the minds of physicians with rheumatism, and may require especial consideration. They are very acid, and may cause considerable irritation. Sponging with a mild alkaline solution, as 1 per cent. sodium bicarbonate, gives relief. The skin should be kept dry with one of the numerous powders that contain talcum, or one made of equal parts of zinc oxide and starch. If the sweating is very severe, atropine may be used in doses of  $\frac{1}{100}$  to  $\frac{1}{50}$  grain.

*Convalescence.* The patient should be kept in bed for some time after the symptoms have subsided—one or two weeks. The diet should be increased to include green vegetables, later eggs, fish, and meat. It should be simple in its character and in the manner of its preparation. It should be sufficient, but not excessive, nor should the patient be teased to stuff by palatable dishes. A change of



environment often helps to establish convalescence, but the patient should not be hurried away too soon or exposed to discomforts in his new surroundings for the mere sake of the change.

*Prophylaxis.* The avoidance of this disease, so lamentable in its consequences, must rest upon our education of the public in hygiene, through the schools and other agencies. The gospel of fresh air must be preached, clean bodies, proper clothing, avoidance of neglect, such as remaining in wet and damp clothing. More than this, parents and teachers must be made to understand the meaning of chorea, sore throats, stiff necks, and "growing pains" in children, and the results of neglect.

## DECOMPRESSION IN THE TREATMENT OF MENINGITIS.

### LUMBAR PUNCTURE IN THE LIGHT OF RECENT ADVANCES.

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THE diagnostic value of lumbar puncture is so well established that I need not dwell upon it. The therapeutic indications for opening the sacral cistern should be equally plain, yet the surprising fact is that even leading text-books on internal medicine are very indifferent as to its use in meningeal diseases. Thus, Koplik<sup>1</sup> and P. Tchernoff<sup>2</sup> advise lumbar puncture *only* for diagnosis. Dieulafoy<sup>3</sup> says it is of no use in the treatment. Holt<sup>4</sup> is at least fair in saying it does no harm, and it may help greatly. Local clinicians seem to dread lumbar puncture even as diagnostic, because once in a great while some one reports a death after the performance, although such a fatality could easily be avoided. Neisser and Pollack<sup>5</sup> say that internists are astonishingly slow to puncture the spinal arachnoid space, although they have promiscuously punctured every other organ or viscus in the body. Be all this as it may, we must agree that the attitude of some authors has resulted in an undeserved neglect of an exceedingly useful therapeutic agent, which, if employed properly, would save many lives and relieve a great deal of unnecessary suffering on the part of the patients.

A critical study of the genesis of the meningitic symptoms conduces to a better understanding of their mechanism, and, consequently to a more logical treatment. The most prominent features

<sup>1</sup> Jour. Amer. Med. Assoc., April 6, 1907.

<sup>2</sup> Archiv f. Kinderheilkunde, February 1, 1906.

<sup>3</sup> Pathologie Interne, 1904, iii, 686.

<sup>4</sup> Diseases of Infancy and Childhood, 1906, p. 766.

<sup>5</sup> Chirurg. Operations-Lehre, 1906, p. 299.

of meningitis—headache, vomiting, and stasis papillæ—are distinct evidences of increased intracranial pressure, whatever morbid lesions they may be based upon. The relief of that excessive pressure becomes the prime indication for immediate lumbar puncture. As early as 1905 P. Marion<sup>6</sup> held this procedure “an excellent agent of decompression, often curative, always palliative.” Kocher<sup>7</sup> insists upon the causal therapy of excessive intracranial pressure, but it is more humane first to relieve the pressure, and then apply etiological treatment, such as antisera, hemostasis, etc. In meningitis the mechanical effects outweigh the toxic lesions. The damage from the former becomes soon irreparable, while the toxic lesions disappear sooner or later, often completely, even after several weeks of duration. Harvey Cushing<sup>8</sup> lays great stress upon the early decompression in excessive intracranial pressure from whatsoever cause. A review of the pathologic-anatomical lesions in meningitis will convince any trained observer of the preventability of these irreparable morbid changes. Energetic prophylactic decompression would reduce to a minimum such disastrous results as optic neuritis, deafness, oculomotor disturbances, and some psychopathies, all of which are due to the mechanical effects of the excessive intracranial pressure. Stieren<sup>9</sup> favors decompression as soon as a diagnosis of excessive intracranial pressure is made, and only then employs medical treatment. The weight of evidence favors the mechanical theory of stasis papillæ, such as advocated by Horsley, Cushing,<sup>10</sup> Spiller,<sup>11</sup> Allen, and others.

Personally I agree with those observers who accept the physical mechanical genesis not only of optic neuritis, but of the totality of the meningeal symptoms. They are avoidable, provided we use decompression early enough. The diagnosis of meningitis depends upon the timely recognition of pressure symptoms. This implies a careful analysis of the findings in the case. Meningitis must be suspected earlier than hitherto. I have elsewhere insisted upon the value of repeated careful blood examinations in this class of cases.<sup>12</sup> Total and differential leukocyte counts will furnish us with very valuable information in the early diagnosis of intracranial hyperpressure. Spiller thinks that when we learn to distinguish between the increased intracranial pressure of inflammatory origin and that of non-inflammatory nature, trephining (decompression) will be more advantageous. The possibility of recovery from meningitis has never been denied, but the consensus of text-book writers and of general experience have discredited it so much that we should not

<sup>6</sup> *Chir. du Système Nerveux*, Paris, 1905.

<sup>7</sup> *Encyclopedie der Gesamten Chir.*, 1901.

<sup>8</sup> *Johns Hopkins Hosp. Bull.*, March 1, 1905.

<sup>9</sup> *Surgical Interference in Choked Disk*, *Ophthalmic Record*, March, 1908, p. 139.

<sup>10</sup> *Cerebral Surgery*, etc., *Jour. Amer. Med. Assoc.*, January 16, 1909, p. 184.

<sup>11</sup> *Internal Hydrocephalus*, *Jour. Amer. Med. Assoc.*, April 13, 1907.

<sup>12</sup> *The Leukocytes in Meningitis*, *Chicago Med. Recorder*, November, 1908.

wonder when Kaufman,<sup>13</sup> in his last edition, says of tuberculous meningitis "it is nearly always fatal." Up to now, the actual recoveries from tuberculous meningitis have been confined to a few text-book reports, although several experienced pathologists told me personally of postmortem findings justifying the retrospective diagnosis of preceding healed meningitis. In those cases, of tuberculous or other nature, when the meningitis is neither a terminal process of a generalized infectious disease, nor an accessory part of an actual serious malady, the outlook should be very good, provided, of course, decompression be early resorted to. Furthermore, I believe that in the near future we shall be able to report a great many cases of meningitis, tuberculous as well as others, with prompt and full recovery. I am convinced that the cases here reported will not remain in the literature as isolated facts, and that the field opened by Jaboulay, Horsley, Cushing and Frazier,<sup>14</sup> Spiller,<sup>15</sup> and Bordley will yield a goodly crop of results.

I feel that meningitis in general, and tuberculous meningitis in particular, has an enormous mortality simply because we allow it to have its way until the lesions produced during our extreme passivity have become irreparable. Theoretically, as I have held for years, a simple meningitis is curable by the timely removal of the excessive intracranial pressure. This has been realized in practice, as shown by the following cases, of which three occurred in my own practice and one case in that of Dr. C. A. Erickson.

CASE I.—Record 1879. September 22, 1908. The patient was seen also by Dr. I. A. Abt and Dr. M. Kahn.<sup>16</sup> The case was treated as one of tonsillitis during the first thirty-six hours. The diagnosis of meningitis was confirmed by lumbar puncture on the fifth day of the disease; 62 c.c. of very clear fluid, escaped under marked pressure. Microscopically, it was negative. Culture and animal experiments were negative. Examination of the blood: 10,200 white corpuscles. The differential count was: polynuclears, 61.4 per cent; small mononuclears, 27.6 per cent.; large mononuclears, 8.5 per cent.; eosinophiles, 0.5. The prognosis was bad before decompression, but the patient began to improve immediately after the lumbar puncture. No other therapy was used.

*Resume.* The case is one of serous meningitis, cured by lumbar puncture alone. The patient is in excellent health now.

CASE II.—Record 1894. January 8, 1909. Eda R., aged six years. Was seen with Drs. M. Bacon and C. M. Piper. Only child, thin and tall. Healthy enough as a baby. Intermittent bronchitis in childhood. Measles one year ago. In good health then until three days ago, when two hours after a fall while roller skating

<sup>13</sup> Spez. pathol. Anatomic, Berlin, 1907.

<sup>14</sup> Cerebral Decompression, Jour. Amer. Med. Assoc., September 1, 1906.

<sup>15</sup> Palliative Treatment for Brain Tumors, Jour. Amer. Med. Assoc., January 29, 1909, p. 272.

<sup>16</sup> Reported in Chicago Med. Recorder, November 1, 1908.

began to complain of headache and nausea which kept getting worse. Vomiting at random. Patient feverish and restless, at first, but rather drowsy in last twenty-four hours.

The child was found in dorsal decubitus, with knees flexed. The head was retracted and opisthotonos quite marked. Rigidity of the spine and the Kernig symptom were pronounced. There was slight ptosis of both upper lids, yet no squint. Pupils normal. Child partially conscious, but rather dull and drowsy. Temperature, 102.8°; pulse, 120; respirations, 30. Moderate tonsillitis. The examination of the skin, joints, lungs, heart, and abdomen was negative. The leukocytes were 40,000 whites (two counts). Differential: polynuclears, 86.3 per cent.; small mononuclears, 9.9 per cent.; large mononuclears, 3.8 per cent.; eosinophiles absent. Lumbar puncture: 45 c.c. of very clear fluid, sterile on microscopic examination, but showing moderated polynucleosis (70 per cent.).

The child improved very slowly during the next four days. On the second day after the lumbar puncture, distinct signs of pneumonia over the right upper lobe; on the fourth day a double otitis media purulenta appeared. Nevertheless, under good nursing, etc., the patient improved so that a week after the puncture, that is, eleven days after the onset, she was able to sit up in her bed for her meals, and had normal temperature.

*Resume.* A case of undetermined meningitis, but probably of influenzal nature (leukocytic formula, pneumonia, and otitis media). Improvement occurred after lumbar puncture and progressed to complete recovery. The patient is in good health now.

CASE III.—Record 2007. Seen with Dr. M. Kahn, January 14, 1909. Julius G., aged four years, well built, well nourished, always well until two days ago, when he took sick suddenly with convulsions, fever, vomiting, and constipation. These symptoms increased in severity until the patient presented the following: half sitting in bed, conscious though a little dull, face flushed, cephalalgia, and random emesis. Slight left ptosis. Head well retracted, neck quite rigid and tender, vertebral column stiff, Kernig symptom manifest. No automatic movements. Temperature, 103°; pulse, 100; respirations, 30. Lungs, joints, throat, and abdomen negative. Lumbar puncture: 70 c.c. of a rather opalescent fluid, under marked pressure, showing 66 per cent. of polynuclears, and 33 per cent. of mononuclears. A cocobacillus with the microscopic features of the Pfeiffer influenza bacillus was found. Injection of 12 c.c. of the fluid into a guinea-pig remained negative. Leukocytes, 22,500 total whites. Differential count: polynuclears, 69 per cent.; small mononuclears, 26.5 per cent.; large mononuclears, 4.5 per cent.; eosinophiles absent. There was mixed polynuclear and lymphocytic leukocytosis.

*Resume.* Acute meningitis, probably influenzal, with very rapid recovery after decompression. The patient is in good health now.

CASE IV.—Report kindly furnished by Dr. C. A. Erickson. Boy, aged seventeen years, with negative antecedents except for suppurating cervical glands in early childhood, and a Neisser infection two years ago. Fell two stories several years ago, but did not injure himself. Initiated into a fraternal society just before the onset of the disease.

About seven weeks ago, with occipital headaches, there was occasional vomiting, loss of appetite, constipation, lack of ambition, loss of weight. Symptoms aggravated progressively, and patient became mentally dull, somnolent, and irritable. He was first seen on May 19, 1909. Temperature was normal; pulse, 46; respirations normal; urine negative. Leukocytes, 14,800. May 20, 1909, he was seen in consultation by Dr. A. R. Edwards. The patient was in opisthotonos, with neck rigid and head retracted. Kernig symptom, diplopia, somnolence, and severe headache were present. The pulse was 50, the temperature normal.

A diagnosis of tuberculous cerebrospinal meningitis was made. Lumbar puncture: 100 c.c. of slightly cloudy fluid, under marked tension; cultures sterile; sediment chiefly lymphocytes. Three days afterward the headache, the vomiting, and the somnolence had entirely disappeared.

May 21, 1909. Left arm, Pirquet showed a markedly positive reaction. Leukocytes, 14,400; temperature, normal; pulse, 60. Patient improved rapidly, but on June 6, 1909, a second lumbar puncture became necessary on account of headaches and vomiting for two to three days previously; 60 c.c. limpid fluid removed. Since then the patient has improved very greatly, and is now apparently in perfect health.

*Resume.* A case of tuberculous meningitis, with recovery. Lumbar puncture, as the only therapeutic measure used in this case, must be considered curative. The removal of intracranial hyperpressure, that is, decompression, was accomplished promptly and thoroughly by means of two consecutive lumbar punctures.

SUMMARY. 1. The semeiology of meningitic symptoms is identical with that of pressure phenomena.

2. The infectious toxic or toxic infectious factor in meningitis has been overrated hitherto, and the mechanical element of this clinical picture has been neglected.

3. The early diagnosis of meningitis depends mainly upon the recognition of actual or suspected intracranial hyperpressure, the removal of which becomes at once the foremost therapeutic indication.

4. Decompression by means of lumbar puncture is feasible in the vast majority of cases, because the aqueduct of Sylvius is seldom totally occluded.

5. The fact that Quinke originated lumbar puncture for the removal of intracranial hyperpressure gains additional value in the light of the recent studies of Harvey Cushing, Spiller, Frazier, Horsley, Bordley, Theodore Kocher, and others.

6. There are several reasons for the enormous mortality of tuberculous meningitis: first, the injury to the brain, due mainly to pressure, causing a degenerative encephalitis; second, the co-existence of advanced tuberculosis elsewhere in the body, usually in the lungs; and third, the occurrence of miliary meningeal tuberculosis, as a terminal infection in such diseases as nephritis, cirrhosis of the liver, etc.

7. Tuberculosis of the cerebrospinal meninges owes its danger to the mechanical effects produced by the excessive pressure upon the medullary centres or the gray matter, not to its infectious character, for, as we well know, tuberculosis elsewhere has a remarkable tendency to self-cure.

## ESSENTIAL PENTOSURIA.<sup>1</sup>

BY SOLOMON SOLIS COHEN, M.D.,

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THE old dictum that life is the chemistry of carbon receives additional illustration in the anomalous condition known as pentosuria—the presence in the urine of the pentatomic form of sugar. It constitutes as yet little more than a clinical curiosity, but suggests many important questions, whose answers, when found, will doubtless be illuminating as to certain dark corners of the field of metabolism.

Pentose is a species name rather than an individual designation. It is applied to a group of some eleven monosaccharids, having the general formula  $C_5H_{10}O_5$ , and thus differing, by one carbon atom and the elements of a molecule of water, from dextrose, levulose, galactose, etc., which, containing six carbon atoms in the molecule, are termed hexoses. But this apparently slight chemical difference is of considerable physiological and pathological importance. The sugar which appears in the urine in diabetes mellitus is dextrose; and, as we all know, its presence usually indicates a profound and often dangerous disorder of metabolism, associated with distressing symptoms and having a somewhat uncertain dependence upon more or less definite structural lesions. While hexosuria is thus potentially and often

<sup>1</sup> Read at a meeting of the College of Physicians of Philadelphia, May 5, 1909.

actually grave, pentosuria, on the other hand, is essentially mild. It is unaccompanied with the polyuria, polydipsia, and bulimia of saccharine diabetes; it is not characterized by emaciation or by obesity; and, so far as yet appears, is unattended with special liability to pyogenic and other infections or with the risk of acid intoxication. Of its possible association with definite tissue changes or circulatory disturbances nothing is known.

Urinary dextrose is optically active; as the name implies, it rotates the polarized ray to the right. Being a reducing aldose, it is commonly recognized by its power to precipitate metals or their oxides from solutions of metallic salts, especially those of copper and bismuth when heated with an alkali. It is fermentable with yeast. These properties are manifested by the hexoses in general, as well as by the disaccharids—for example, sucrose and maltose—which contain twelve carbon atoms and may, by the hydrolyzing action of dilute mineral acids, be made to take up the elements of an additional molecule of water and separate into two hexose molecule groups. The pentoses are likewise reducing aldoses. They behave much like dextrose with the bismuth test of Boettger, but the reduction of metallic bismuth is usually incomplete and the precipitate is brown or gray, rather than an absolute black. With Fehling's solution, they give a peculiar reaction, producing somewhat suddenly, after some minutes' boiling, a heavy greenish or yellowish or orange-colored precipitate in place of the red or salmon-colored oxide with whose gradual development we are familiar. While decomposable by the action of certain bacteria, and especially the intestinal flora, they do not, however, ferment with yeast, and their bacterial decomposition is not attended with the evolution of gas. Consequently, in the examination of a specimen of urine which reduces bismuth imperfectly and gives an anomalous or incomplete copper reduction, the failure to ferment, more especially if polariscopic examination shows the reducing substance to be optically inactive, should direct attention to the possibility of the presence of a pentose. Diabetes mellitus is in such instances excluded; but other chemical tests must be made before the identity of the reducing, non-fermentable substance can satisfactorily be established. The most difficult discrimination is that between glycuronic acid and pentose. In the case which I report herewith I availed myself of the chemical skill and knowledge of Professor Charles H. La Wall to make this discrimination, and he has kindly consented to report the results of his tests and to explain their significance. While optical inactivity is almost conclusive, both against dextrorotatory glucose and levorotatory glycuronates, it must not be forgotten that many of the pentoses are optically active; and at least one of these has been known to appear in the urine. The crucial test is the recognition of the melting point of the crystals of pentosazone produced by

the action of phenylhydrazin. Spectroscopic examination, moreover, shows different positions of the absorption bands of the substances produced by the action of various reagents with glycuronic acid, dextrose, and the pentoses.

The pentose group of saccharids—or, more correctly, a group of anhydrides, called pentosans, which bear the same relation to the pentoses that starch, for example, bears to dextrose—is widely distributed, if not universally present, in the vegetable kingdom; being found in fruits, leaves, stems, and roots. The legumens and, among fruits, the pear, are especially rich in pentosans. The nucleinic acid of the embryos of wheat was found by Osborne and Harris to contain three molecules of pentose to each 4 atoms of phosphorus. Pentose has been demonstrated by Kossel and Neuman in the nucleinic acid of yeast, and Bendix, as well as Aronson, has found it in bacteria, including pathogenic forms, as tubercle and diphtheria bacilli. The most common forms of vegetable pentose are those termed l-arabinose and l-xylose. In the animal body, pentose was first discovered by Hammersten as a constituent of the nucleoproteid of the pancreas. The substance thus discovered has been identified as l-xylose. Since then various observers have demonstrated its presence in the liver, the thymus, the thyroid, the spleen, the kidney, the muscles, the brain, and the mammary gland, and it is, in general, supposed to be a persistent constituent of the nucleus; so that it is most abundant in those tissues that are rich in nuclei. Nevertheless, the whole amount contained in an ordinary adult human body has been calculated as not more than about 10 grams.

Pure pentose, when given to man or the carnivora by the mouth or injected into the blood, may be in small part assimilated; but it is usually, for the most part, rapidly excreted in unaltered form in the urine. Nevertheless, large quantities of pancreas or of vegetable foods containing pentosans may be ingested without the production of an alimentary pentosuria; probably on account of the slowness with which the saccharid is set free from its proteid combinations. The discordant results obtained by various observers in regard to the quantities of pentose recoverable from the feces and urine when pure xylose or pure arabinose has been administered by the mouth, are to be attributed in some measure to its decomposition, with the formation of lactic acid and alcohol, by the intestinal bacteria; and this process probably tends also to prevent alimentary pentosuria under ordinary conditions. While the pentosans and pentoses seem to play an important part in the nutrition of herbivora, no animal or vegetable enzyme that will hydrolyze pentosans has been demonstrated with certainty; and the physiological questions concerning their assimilation and utilization are as yet quite unsettled.

When alimentary pentosuria is induced by the feeding of pure



pentose, the form that appears in the urine is the dextrorotatory l-arabinose,<sup>2</sup> whereas that which appears in essential pentosuria is the optically inactive r-arabinose. The apparent exception reported by Luzzato is attributed by some critics to a transient alimentary pentosuria accompanying the essential form. Urinary pentose is supposed to be excreted in combination with urea, as an arabinoseureid. To this fact is to be attributed the slow reduction giving rise to the peculiar reaction with Fehling's solution; for the sugar must first be set free from its proteid combination by the action of the heat and alkali; and this decomposition occurs only after some minutes' boiling. In fact, in the first examination of the specimen from my own case I was unable to get any response to Fehling's test until I had added a decided excess of alkali.

Pentosuria was first clinically recognized in 1892 by Salkowski and Jastrowitz. The patient happened to be a person addicted to morphine, and his drug habit was supposed to have some causal connection with the condition. This idea, however, has been disproved. In 1895 Blumenthal reported two additional cases from Salkowski's laboratory. Since then a number of cases have been reported, most of them, however, from the First Medical Clinic in Berlin and Salkowski's laboratory. Neuberg identified the urinary pentose as r- or racemic arabinose, which is optically inactive, but may be decomposed into dextrorotatory and levorotatory constituents. Luzzato, however, found the pentosazone obtained from the urine of his patient to be slightly dextrorotatory, corresponding in this respect with the pentosazone of the l-arabinose of the vegetable kingdom. In my case a dextrorotation of scarcely 1° was found on one occasion only. The significance of this will be discussed later.

Three varieties of pentosuria have been recognized:<sup>3</sup> (1) *Alimentary pentosuria*, in which the phenomenon follows the ingestion of food rich in pentose-producing substances. (2) *Complicating pentosuria*, in which the urine contains both pentose and hexose—the cases being actually diabetes mellitus, and the small quantities of pentose transiently present having no known clinical significance.

<sup>2</sup> The letters *d*- and *l*-, as prefixed to the names of the various pentoses, are as likely to be confusing to other physicians who do not happen to be expert chemists, as they were to me until I learned the facts. One would naturally suppose that *d*-arabinose is dextrorotatory and that *l*-arabinose is levorotatory; but the exact contrary is the case. The letters do not indicate the optical activity of arabinose, xylose, etc., but that of the hexose molecules with which the pentoses are respectively chemically homologous.

<sup>3</sup> The substance obtained by Cammidge from the urine of patients having pancreatic disease is also supposed to be a pentose. In a recent case of my own showing a slight Cammidge reaction glucose was excreted for a few days; and then a reducing, non-fermentable substance, not yet identified. A similar series of phenomena occurred in the case of an obese woman of diabetic and carcinomatous heredity, and marked vasomotor ataxia of the menstrual variety; suggesting a possible origin in pancreatic circulatory disturbance. This case is reported in my paper on "Visceral Angioneuroses," in the Transactions of the Association of American Physicians, 1909.

Similar to these cases are the instances of experimental pentosuria found to accompany the diabetes mellitus of dogs deprived of the pancreas or poisoned with phloridzin. (3) *Essential pentosuria*, in which the excretion of pentose is persistent, independent of diet, and not associated with diabetes mellitus. It cannot be said, nevertheless, that in essential pentosuria there is no association with hexosuria. The relation, however, is the reverse of that obtaining in complicating pentosuria. It is now the dextrose that appears transiently and in minute quantities, and even this has been recorded in but a few cases, of which my own appears to be one.

According to T. C. Janeway,<sup>4</sup> who, in 1906, reported two cases of essential pentosuria in brothers, there had been previous to his report but seventeen indubitable cases placed upon record, of which one came from Italy and two from Norway, but none had been found in British, French, or American literature. So far as I know, the present is the fourth case observed, and the third case to be placed upon record, in the United States. Added to the seventeen cases collected by Janeway, with the two reported, and two others (unpublished) alluded to by this author, it would make twenty-two in all. I have not searched the literature since Janeway's report, and there may be a few more. At all events, the total number of cases recorded in the seventeen years elapsing since the first clinical recognition of the condition, has not reached forty. For this reason, isolated cases are still worthy of report.

My patient is a married man, a native of one of the middle Western States, aged fifty years. He has never had any venereal infection. He uses alcohol rarely and tobacco moderately. He is a leading member of the bar of his State, and is frequently required to appear in the supreme courts of other States and of the United States. It may, therefore, fairly be said that he has been engaged for many years in arduous, sometimes exhausting, mental labor; and, if we consider the strain of travel and of pleading, in physical labor as well. However, he has the vacation habit well established, and except for an occasional European trip, usually spends his summers in the woods or mountains, or on the Maine Coast, tramping, boating, fishing, hunting, or loafing, as the environment and his mood may suggest. When at home he rides and golfs as opportunity offers. He does not, therefore, strictly speaking, lead a sedentary life. He has recently—that is to say, for some four or five years past—been actively engaged in a movement for reform in the government of his city; and has had in connection therewith the burden of preparing important legal cases against a number of eminently respectable citizens. It is to be supposed, therefore, that he has been under a severe mental strain.

While he exhibits some of the signs of vasomotor ataxia, he is not what is commonly termed neuropathic; and there is not in his

<sup>4</sup> AMER. JOUR. MED. SCI., 1906, cxxxii, 423.

family any history of neuropathic, arthritic, malignant, tuberculous, or diabetic affection. Cutaneous affections have been present.

He first came under my care about fifteen years ago with symptoms of subacid, gastro-enteric indigestion. Recovery took place under lavage, gastric faradization, and regulation of diet and exercise. The urine showed an excess of indican, as well as of uric acid, urates, and oxalates, but contained no albumin, sugar, or casts. An attack of furunculosis some years later made me study the urine carefully and persistently for glucose, but none was found. The patient has had from time to time brief periods of indigestion, sometimes a transitory constipation; but there has been no significant ailment of any kind. He has had periods of genuine and well-earned fatigue, but no neurasthenia. He has seen me at least once in every year, often more frequently; and I have probably examined his urine three or four times in each year, finding neither albumin nor sugar. He has also consulted, when necessary, a leading physician of his home city, one of my own pupils, whom I have associated with me in the case. It is unlikely, therefore, that any pathological occurrence would go long unnoticed.

In March, 1908, a life insurance examiner postponed his application, and he learned indirectly that it was on account of the urinalysis—albumin was said to be present. There was no suspicion, apparently, of sugar. The local physician examined the urine and found no albumin, but an anomalous reduction with Fehling's solution. He suggested that diabetes might be impending, but in the total absence of symptoms hesitated to make the diagnosis. A specimen of urine, taken from a twenty-four-hour collection amounting to 1500 c.c., was sent to Philadelphia. I found it to be clear, amber in color, 1023 specific gravity, acid in reaction, giving a brownish precipitate with bismuth subnitrate and potassium hydroxide, a greenish-yellow precipitate with Fehling's solution, and no gas upon attempted fermentation with yeast in Einhorn's saccharometer. There was no albumin; casts were not detected. A few leukocytes formed the only microscopic finding. Suspecting pentose, I enlisted Professor La Wall's cooperation, and, studying the specimen with him, found it to give all the pentose reactions, but in exception to be slightly dextrorotatory. A few days later the patient himself arrived. Careful physical examination showed nothing abnormal except a very slight enlargement of hepatic dulness, which had been present for some four or five years, and a very slightly increased arterial tension, not high enough, however, to indicate pathological change in the arteries. The blood was normal to microscopic and color study. The eye-ground had been examined by a local oculist, and was reported to be normal. The patient had gained some twenty pounds in weight during the last five years, but was not pathologically obese.

I have, in conjunction with Mr. La Wall and the local physician, kept the patient and the urine under observation, more or less closely, ever since; that is to say, for more than a year. Twice during that time he has complained of lassitude and indisposition to work—symptoms quickly disappearing after a few days at Atlantic City, or the brief administration of lecithin or glycerophosphates. Milk diet, flesh diet, diet with and without the ordinary carbohydrates, and diet with and without substances rich in pentosans have been instituted; for brief periods only, it is true, as the patient's activity does not lend itself to overmuch regulation or restriction. There has been practically no change in the urinary findings, except that although Mr. La Wall has not again found any dextrorotation, the local physician in February of this year did find, on one occasion, a few bubbles of gas; and on another, a reading of 0.25 per cent. by gaseous column, in Einhorn's saccharometer. I did not have either of the specimens, and cannot confirm the observation; but I know the observer to be accurate. This would seem to indicate some transient complicating excretion of a fermentable sugar [and, since the paper was read, a small quantity of hexose has again been found, as set forth in the footnote].

There is no instance on record of the transformation of pentosuria into diabetes, yet while knowledge remains so limited, care is necessary. I therefore thought it well to test dextrose assimilation more particularly. For this purpose I gave the patient, by the mouth, on each of two successive days, 100 grams of the glucose of pharmacy, in two portions; and with Mr. La Wall examined the total urine of the forty-eight hours. In this there was no trace of any excreted hexose, but pentose was found as before. No excess of indican has been found in the pentose-containing urine, although this was occasionally present before the pentosuria was discovered. The excretion of urea continues around 3 per cent. The chlorides in the late specimen were 0.94 per cent., or about 15.46 grams. The phosphates, estimated as  $P_2O_5$ , were 0.3 per cent., or 4.8 grams, a slight increase over the normal average. The total sulphates, being 0.31 per cent., or 5 grams, of which 0.3 per cent. represents preformed salts, show also a slight increase; while the rather low ratio of conjugate to fixed sulphates, 1 to 30, especially when taken in connection with the low indican content, would show a relative absence of intestinal decomposition. Bacterial study of the feces is therefore desirable, for a question is raised as to the possibility of absence or partial destruction of intestinal bacteria as a factor in the production of the pentosuria. Whether or not this study can be carried out, I do not know, but it calls for attention. The salol test does not indicate any failure of the secretion that splits this drug.

I have not specially experimented with the feeding of sucrose,

levulose, lactose, etc., or with any pure pentose; but hope to have the opportunity to make these and other observations from time to time, as the patient finds opportunity to visit Philadelphia, or we succeed in enlisting expert chemical assistance in his own city.<sup>5</sup>

The diagnosis of essential pentosuria is established by the persistence of the pentose excretion and by the absence of other symptoms.

The chief importance of this condition at present, apart from the interesting questions in physiological chemistry to which it gives rise, is its liability to be mistaken for diabetes mellitus, or, at all events, for glycosuria. Indeed, most of the cases hitherto recorded have been so mistaken until coming under the care of a physician familiar with the fact that pentose may appear in the urine, when the diagnosis has been corrected.

Pentosuria is apparently an intractable condition, but occasions very little inconvenience, and, so far as yet appears, is devoid of danger to life. About the worst thing that can happen to the patient is to have the condition mistaken for glycosuria and to be restricted in diet accordingly. This is very likely to cause loss of strength as well as of flesh. When, however, the true nature of the case is recognized and a diet properly adapted to the individual conditions instituted, the patient rapidly recovers from this loss and appears to be normal in every respect, except for the urinary findings. The only medicament which, from report, seems to influence the condition favorably, is arsenic. In the case of my own patient no medication has as yet been employed.

No light is thrown upon the metabolic fault concerned in the production of pentosuria by the habits, age, sex, vocation, nationality, or social and climatic environments of the patients as thus far recorded. Their ages vary from twenty to sixty-five years; they are of both sexes (although at first only males were reported), and their occupations, birthplaces, and environments have been as little similar as banking and farming; idling and practising law; wealth and poverty; Germany, Norway, Italy, and the Eastern and middle Western regions of the United States. Some of them have been morphine takers, some cocaine users, some neurasthenics. Two have been vegetarians. Quite a few cases have been

<sup>5</sup> Our patient, however, informs me that I have "overestimated his zeal for scientific research." He consented, nevertheless, to visit Berlin while in Europe this summer, and to see Dr. Jastrowitz, who writes as follows:

"Both Professor Salkowski and I, can, from careful studies, entirely independent of one another, confirm your diagnosis of pentosuria. The first time that the patient brought his urine to me, I found, in addition to pentose,  $\frac{1}{2}$  per cent. of hexose, but although I had the urine of various periods brought to me later, as well as the entire twenty-four hours' quantity after diets rich in carbohydrates, I could not find any increase of hexose, but, on the contrary, only occasional traces of it; nor did the pentose seem to be notably increased after he had eaten many cherries (kirschen)."

observed in brothers, or in sisters, or in brother and sister; so that there seems to be some indication of a family tendency.

As the pentose continues to be excreted, even when the patients are put upon exclusive milk diet, and rarely seems to be increased notably, even by a diet of pancreas or pears, it is somewhat difficult to attribute the excretion of pentose to failure in assimilation of foodstuffs. The theory that pentosuria results from the breaking up of the pentose-proteid combinations of the body tissues has in its favor the discovery of arabinose in the blood of one or two patients; but against it, on the other hand, is the fact that the body pentose is l-xylose and the urinary pentose r-arabinose. Granting, however, that transformation of these isomers could be explained if we knew the intimate mechanism of the metabolic failure, there remains the still greater difficulty that the average daily urinary excretion in the cases thus far observed has been from 5 to 20 grams of pentose, whereas the entire body contains but about 10 grams. The problem, therefore, still awaits solution.

## THE CHEMICAL EXAMINATION OF A SAMPLE OF URINE CONTAINING PENTOSE.<sup>1</sup>

BY CHARLES H. LA WALL, PH.M.,

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THE urine, which had a specific gravity of 1023 and a yellow color, first attracted attention by the abnormal reaction produced when heated with Fehling's solution, which was not reduced to copper oxide, as is the case when the ordinary carbohydrates are present, but which produced a characteristic greenish turbidity and eventually a yellow precipitate. The fermentation test gave negative results, while a pronounced reduction was obtained by means of Boettger's test with bismuth subnitrate and solution of potassium hydroxide. A more extended examination, therefore, seemed desirable, and about a pint of the urine was furnished, with a request for an exhaustive investigation.

The first test applied was the alphanaphthol test, which is a group test for carbohydrates in general. It is applied by adding to a suspected sample of urine a few drops of a 10 per cent. alcoholic solution of alphanaphthol and then superimposing this liquid upon concentrated sulphuric acid. In the presence of any carbohydrate a violet zone is produced. This test resulted positively.

<sup>1</sup> Read at a meeting of the College of Physicians of Philadelphia, May 5, 1909.

The Fehling test was then applied, with the result as previously stated. The reaction showed a greenish turbidity, which was succeeded by a yellowish precipitate, wholly unlike the normal copper reduction.

The Boettger test, with bismuth subnitrate and solution of potassium hydroxide, showed a marked reduction to the dark-colored metallic bismuth.

The indigo carmine test for dextrose gave negative results.

A fermentation tube showed no evolution of  $\text{CO}_2$  after twenty-four hours.

A polariscopic examination of the sample showed that it was optically inactive.

The phenylhydrazine test was then applied as follows: A clean, dry, six-inch test-tube was filled to the depth of one-half inch with phenylhydrazine hydrochloride, one-half inch of dried sodium acetate was added, and the tube filled to half its capacity with the urine and immersed in a bath of boiling water for two hours. Upon cooling the contents of the tube a voluminous deposit of yellow crystals took place, which, when examined microscopically, were found to be in stellate tufts of acicular crystals, resembling somewhat the groups produced by dextrose or levulose, but different in the character of the individual crystals, which seemed to be more slender in proportion to their length.

Several additional tubes of the crystals were prepared in a similar manner, and some of the crystals were collected and purified by recrystallization. During this purification it was noticed that the crystals were much more soluble in hot water than is the case with ordinary dextrosazone. The purified crystals were found to have a melting point of  $157^\circ \text{C}$ . This corresponds closely to the melting point of pentosazone; which substance was found by Salkowski and Jastrowitz to have a melting point of  $166^\circ$  to  $168^\circ \text{C}$ . when pure, but from  $156^\circ$  to  $160^\circ \text{C}$ . when obtained from urine. The melting point of dextrosazone (and levulosazone) is  $204^\circ$  to  $205^\circ \text{C}$ .

Several subsequent experiments upon fresh samples of material confirmed the melting point of the crystals, and the various specific tests for pentose were applied. Tollen's test, which is carried out by heating a solution of phloroglucin in hydrochloric acid and adding to the hot solution a small quantity of the urine, continuing the heat upon a water bath for some time, gave positive results in the shape of a cherry-red liquid which became cloudy upon cooling.

As glycuronic acid also responds to this test, further confirmation was obtained by applying the orcin-hydrochloric acid test, which is carried out similarly to the one previously described, using orcin instead of phloroglucin. In the presence of pentose a bluish-green color is developed, which is dissolved out by shaking with amyl alcohol. Positive results being obtained by this test,

thus negating the presence of glycuronic acid, there seems to be no further doubt that there is exhibited in this sample of urine a well-developed case of pentosuria, as precisely the same results as above described were obtained in a specimen of urine from the same individual examined eleven months after the first report.

## ADIPOSIS DOLOROSA WITH MYXŒDEMATOUS MANIFESTATIONS.

BY HEINRICH STERN, M.D.,  
OF NEW YORK.

ADIPOSIS dolorosa is not a disease entity, but a condition characterized by a more or less definite symptom-complex. The two phenomena which are always encountered are irregular deposits of fat in the subcutaneous tissues, and pain in the fatty swellings. The other characteristics which are usually but not inevitably present are weakness, mental disturbances, and disorders of menstruation. There are other symptoms which may occasionally supervene, as sensory disturbances, headache, and diminished perspiration. It is an affection occurring in the vast majority of instances in women, generally setting in between the fortieth and fiftieth years of life, at a period when the menstrual functions are more or less deranged or the menopause has already become established. As but fifty cases of the condition have been reported in literature since Dercum first described the symptom complex in 1888, every additional instance of it should be recorded, especially if it presents certain features of myxœdema, as does the case narrated in the following:

Mrs. E. W. was referred to me by Dr. J. Gutman, of New York City, on April 21, 1908. The patient is a native of Roumania, belongs to the Hebrew race, is forty-two years old, married for eighteen years, and has never been pregnant. Her immediate family history is good; alcoholism, insanity, epilepsy, tuberculosis, or cancer had not occurred in a single member thereof. Her husband has never been affected with any venereal disease. The patient is bright, well educated, and apparently anxious to assist her medical adviser.

Menstruation started in the thirteenth year, but was never profuse. Since puberty the patient has not had an infectious disease necessitating staying in bed. About four years ago she slowly began to grow fat. At present she weighs 224 pounds. For the last year she noticed a progressive weakness, palpitation, and shortness of breath on even the slightest exertion, and, as she herself explains, "tiredness of soul and body." She has had non-



pitting œdema of the face, legs, and feet, and suffers with paroxysms of pain in the entire legs, especially in the calves and the posterior portions of the thighs. The pain becomes excruciating on standing, and even more so when walking. There are also pains in the region of the neck and chest, but they are of a more fleeting nature. For the past two years the perspiration is noticeably reduced, even during hot weather, and the hair has been falling out in a marked degree.

*Examination.* The patient has an apathetic, bloated physiognomy, is well developed, and has large diffused deposits of fat over the abdomen, shoulders, and back, but desultory accumulations of fat are particularly noticeable just above the ankles, on the posterior and inner sides of the calves, the inner sides of the knees, and the external sides of the thighs and over the lower portion of the buttocks. While there is but little pain elicited on pressure upon the abdominal, cervical, and dorsal fat layers, the sensitiveness of the fat deposits in the legs is very pronounced when pressure is applied. The lower the location of the fat deposit the greater proves the pressure pain. The most acute pain is induced in the fat pad around both ankles; the pain induced in the fat deposits on the inner side of the knees and over the calves is less sharp, but much more intense than the induced sensitiveness in the fat masses of the thighs and buttocks. There are no lumpy fat deposits in the upper extremities. The circumscribed fat masses in the lower extremities are quite firm and do not pit when pressed upon. The integument directly over and surrounding the circumscribed fat deposits is soft and pliable, having retained more or less its normal character. In the face, however, the skin is rather firm and inelastic, and exhibits areas of distinct roughness. There is a slight enteroptosis, and the flabby panniculus hides the external genitals. The respiratory organs show nothing abnormal; there exists without a doubt a fatty infiltration of the heart. No cardiac lesion besides this is discernible, but the second aortic sound is distinctly accentuated. The blood pressure over the radial artery is 90 mm. Hg. by Potain's instrument. The thyroid gland is not palpable. The cervical and axillary glands are not enlarged, but just above the clavicles there are small superficial nodules which seem to be due to the shrivelling of the skin and the subjacent structures. The liver is normal in size and presents nothing unusual around its lower border. The spleen is not palpable, and its area of dulness appears to be of normal extent. The stomach is somewhat ptotic, but not enlarged. There is a marked pressure pain in the region of the descending colon and the sigmoid flexure; this is undoubtedly caused by hardened feces accumulated therein. The inguinal glands are not enlarged. The temperature, taken by mouth and rectum, is normal. Muscular power is much diminished, and the patient cannot hold the arms extended without much effort. There is greater muscular strength

in the lower extremities, but even a slight exertion causes more or less pain. The patellar reflexes and the tendo Achillis reflex are diminished. The deep reflexes of the upper extremities are sluggish. Babinski's reflex cannot be elicited. There is no tenderness over the nerve trunks. Coördination, sense of orientation, and stereognostic sense seem unimpaired. The ocular phenomena are negative. The percentage of hemoglobin is 70. There are no abnormal urinary features, neither chemical nor microscopic.

A *diagnosis* of adiposis dolorosa with symptoms of myxoedema was entertained.

The *treatment* advised consisted of an anti-obesity diet, thyroid medication, and physical therapeutics, especially vibratory massage and exercise.

May 10, 1908. The patient has executed the prescribed treatment under the supervision of her family physician. Her present weight is  $210\frac{1}{4}$  pounds. She feels weak, but is not discouraged. The pains in the legs continue; they are so severe in the morning that she cannot make any steps, but is compelled to crawl on her knees if she has to move about. Later in the day the pains subside to some extent, and then she is able to take some exercise. The findings of the physical examination do not materially differ from those obtained on the previous occasion. The twenty-four hours' urine amounts to 1200 c.c.; there are no pathological elements contained in it. In addition to the former treatment special exercises for the feet and a supporter for the pendulous abdomen are recommended.

July 15, 1908. The patient has religiously executed the treatment with the aid of her physician. She weighs now  $188\frac{1}{2}$  pounds. She complains of "general weakness from head to feet." She looks exceedingly anemic. The thyroid had to be temporarily withdrawn on account of increased cardiac palpitation and some arrhythmia. The physical examination demonstrates a stronger cardiac impulse. The radial blood pressure amounts to 120 mg. Hg. taken with Potain's instrument. The urine remains unchanged. Glucose in clinical amounts cannot be ascertained. The treatment is continued excepting the thyroid medication, which is to be resumed in a week or two, but in smaller daily doses.

January 4, 1909. The patient presented herself today to show me the beneficial effects of the treatment. Excepting the pallor, which, she says, has always caused her much annoyance since her early youth, she looks very well. She feels strong, and is able to walk from five to eight miles a day; she experiences no shortness of breath on ordinary exercise, but perspires mildly when she walks briskly. The fat bunches have disappeared almost entirely; the neuralgic pains ceased about four months ago; there is no tenderness on pressure on the location of the former fat masses. The skin in the supraclavicular regions and in the face has been quite

tender. She evinces not the slightest mental depression and apathy, but, on the contrary, displays a healthy optimism. Her present weight is 161 pounds.

COMMENTS. The foregoing case is of especial interest for two reasons—the concurrence of adiposis dolorosa with well-marked myxœdematous manifestations, and the synchronous abatement of the symptoms of both affections after thyroid medication and a general anti-obesity treatment.

Symptoms of myxœdema are known to supervene in a certain proportion of the cases of adiposis dolorosa. Dercum's first publication on this subject was entitled "a subcutaneous connective-tissue dystrophy resembling myxœdema," and Henry reported some time later a case under the caption of "myxœdematoid dystrophy." Thus, the possible concurrence of both conditions, or at least a certain resemblance of adiposis dolorosa with myxœdema, was recognized by the early writers on the syndrome.

The instance of adiposis dolorosa under consideration exhibited the following myxœdematous manifestations: Apathetic, bloated physiognomy; history of non-pitting œdema of face, legs, and feet; firm, inelastic, and rough skin in the face (seat of former œdemas); falling out of the hair; non-palpable thyroid, and dermal tumefactions in the supraclavicular areas. This symptom complex alone would prompt the diagnosis of myxœdema, but it was overshadowed, at least for the time being, by the acuteness of that of adiposis dolorosa. The association of the two syndromes is by no means accidental, although it appears that in none of the cases of adiposis dolorosa on record were the myxœdematous features as plentiful and well pronounced as in the case before us.

In view of the frequency of myxœdematous symptoms in adiposis dolorosa, I think we are justified in accepting a kindred cause of both syndromes. That thyroid insufficiency stands at the foundation of myxœdema there can be little doubt; again, some thyroid alteration was found in four out of five cases of adiposis dolorosa which came to autopsy. While the seat of the externally visible pathognomonic symptoms of myxœdema is in the subcutaneous tissues, that of adiposis dolorosa is situated in the fatty structures.

Moreover, the improvement of my case following the administration of thyroid extract seems to evince with certainty that perverse thyroid function was, so say the least, an antecedent. The yielding of both symptom complexes to the same medication again points to their interrelation or their springing from a kindred cause. Thyroid therapy cannot, therefore, be utilized as a test of differentiation between myxœdema and adiposis dolorosa, as some authors maintain, because both syndromes may vanish under its influence, and, as in the present instance, even at the same time. In so far as the pains disappeared in the ratio of shrinkage of the fat bunches, we are justified in concluding that the irritation of the nerve terminals

was either due to mechanical insults on the part of the overgrowth of fat tissue, or to certain fatty acids or products of katabolism exciting the nerve trunks in the vicinity of the fat deposits and stimulating the fat-tissue to further proliferation. In view of the fact that myxœdema occurs without pains in the swellings, it appears that thyroid insufficiency cannot be held directly responsible for the aches and paroxysms in adiposis dolorosa.

## HEMOPHILIA WITH THE REPORT OF A CASE OF TYPHOID FEVER IN A HEMOPHILIC SUBJECT.

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By the term hemophilia we mean a peculiar hereditary anomaly of constitution characterized by traumatic hemorrhages of great stubbornness and also by a conspicuous tendency to spontaneous and repeatedly recurring hemorrhages, subcutaneous, subfascial, intra-articular, intraperitoneal, intrapleural, intracranial, or from the mucous surfaces. The condition, of course, must not be confounded with other pathological states, such as scurvy and purpura, in which there is a marked tendency to hemorrhage; the former is a definite disturbance of nutrition, the latter an acquired condition dependent upon a variety of specific organisms or their toxins. Nor must we confound it with the so-called hemorrhagic diathesis associated at times with certain of the specific fevers, nor with multiple hereditary telangiectasis first described by Osler.<sup>1</sup>

According to Wilson,<sup>2</sup> priority is due Albucasis, an Arab, who died in Cordova A.D. 1107, and in whose writings a well authenticated instance of hemophilia is mentioned. Alexander Benedictus, in 1539, Hochsetter, in 1674, Legg, in the same year, Fordyce, in 1784, and Rave, in 1798, were among the earlier observers. The first American physician to mention the disease was Otto,<sup>3</sup> in 1803, and it was he who applied the term "bleeders" to patients afflicted in this way. He gave the history of a family in which the disease could be traced back 80 years. In 1813 Hay gave details of the Appleton-Swain family, which, it seems, was another branch of the family reported by Otto. In 1817 Buel<sup>4</sup> reported cases in the Collins family, and in 1828 Coates<sup>5</sup> recorded others in a Pennsylvania family. The German school here took up the study, and articles appeared by Nassi, Wachsmuth, Virchow, and

<sup>1</sup> Johns Hopkins Hosp. Bull., November, 1901.

<sup>2</sup> Practitioner, Lond., 1905, lxxv, 829.

<sup>3</sup> New York Med. Repository, 1803.

<sup>4</sup> Trans. Med. and Phys. Soc., New York, 1817.

<sup>5</sup> North Amer. Med. Jour., 1826.

others. Since that time a vast amount of literature has been accumulating, so that at present the mass at our disposal is too great to be given in detail in any brief paper.

**ETIOLOGY.** That the condition is hereditary is agreed by all observers, and Grandidier, in his monograph, calls it "the most hereditary of all hereditary diseases." The transmission may be direct from parent to child, but much more frequently follows a peculiar law, peculiar in that it reveals a remarkable difference in the frequency of incidence in the two sexes, females showing the greater tendency to transmit the disease, while acquiring it themselves but seldom, whereas just the reverse is true in the male sex. For instance, a mother of a family, although she herself has never manifested any hemophilic tendency, despite the fact that she is the daughter of a hemophilic parent, will transmit the disease to the majority of her male offspring, the ratio being about 11 to 1. Statistics show that for about every 13 males so afflicted there is only one female. Nevertheless, the view formerly held that women exclusively transmit the disease has been shown in recent years to be erroneous, and there are to be found in the literature instances in which fathers, themselves bleeders, and also fathers the sons of bleeders, though themselves not bleeders, have occasionally transmitted the tendency. Hence it is now agreed that men descended from bleeder families, whether bleeders themselves or not, occasionally beget hemophilic children, and that women descended from bleeder families, whether bleeders themselves or not, almost invariably give birth to hemophilic children. Lossen,<sup>6</sup> Gocht,<sup>7</sup> and Sahli,<sup>8</sup> in their articles on hemophilia, give very striking and interesting genealogical tables. That the tendency can be transmitted through several generations is well shown by the family tree first described by Grandidier and Vieli, and later by Hosli, in which the transmission was followed through seven generations. In several instances in this family the disease would skip two generations and reappear in the third.

Although heredity is responsible for the majority of the cases of hemophilia, a congenital form also appears to exist. By this is meant that children of parents not themselves bleeders, and who can give no family history of hemophilia, are occasionally hemophilic. These children will transmit the disease to succeeding generations.

So far as race is concerned, Germany furnishes the largest number, England is next, then France, then North America. Russia, Switzerland, Norway, Sweden, Holland, Belgium, Denmark, and East India all furnish one or more families. In the lower animals cases of hemophilia have also been reported. E. A. Weston<sup>9</sup>

<sup>6</sup> Deut. Ztschr. f. Chir., 1905, lxxvi, 1.

<sup>8</sup> Ztschr. f. klin. Med., 1905, p. 264.

<sup>9</sup> Vet. Records, Lond., 1904-05, xvii, 100.

<sup>7</sup> Arch. f. klin. Chir., Band lix.

reports a case of equine hemophilia, and Villemain<sup>10</sup> reports a case in a dog.

Although the actual cause of hemophilia is still unknown, numerous hypotheses have been advanced. Some authors lay stress on marriage between blood relations and maternal impressions as causative influences. Neither view, however, appears to be well founded. Among the many other theories advanced the following may be mentioned: Cohnheim assumed some change in the erythrocytes as explanatory of the condition, but this view has received no confirmation from other observers, and Litten claims to have absolutely disproved its possibility. Immermann<sup>11</sup> held that disproportion between the blood volume and the capacity of the vascular apparatus, resulting in an unusual pressure in the latter, produced the hemorrhages, but against this view is the fact that repeated blood pressure findings in the majority of instances that failed to reveal a tension greater than normal. Oertel,<sup>12</sup> however, expresses himself as in favor of Immermann's theory, and speaks of a hydremic plethora of high degree. Cohen,<sup>13</sup> working along the same lines, but unfortunately with only one case from which to draw his conclusions, suggested a treatment which has for its main object the reduction of the so-called hydremic plethora by means of energetic cataphoresis and diuresis. Von Recklinghausen's<sup>14</sup> hypothesis, that hemophilia is a neuro-pathic diathesis and secondary to vasomotor disturbance, is based mainly upon the observation that neurotic symptoms are frequently seen in bleeders, but, as Litten points out, whether these neurotic manifestations are *post hoc* or *propter hoc* is by no means clear. W. Koch, of Dorpat, believes hemophilia to be merely another manifestation of scurvy, purpura, or similar conditions, and claims that it is a toxic infectious disease, but this theory can hardly be well founded in face of the fact that no specific pathogenic organism has ever been isolated or proved to exist in hemophilic patients. Moreover, it seems most improbable that such agents existing in a parent should fail to appear in the next generation and yet reappear in the following; nor would it be possible to explain in this way the marked discrimination on the part of the organism between the sexes. In the cases in which Kolb, Babès, Gartner, Tizzoni, and Giovanni demonstrated bacteria, and referred to as instances of hemophilia of the new born, the hemorrhages were probably analogous to those so often seen in septic and other infections, and should be classed as toxic instead of hemophilic hemorrhages. In a case in which

<sup>10</sup> Jour. de méd. vét. et zootech., Lyon, 1904-05, viii, 590.

<sup>11</sup> Ziemssen's Handb. Pathol. u. Ther., 1879, xiii, 2.

<sup>12</sup> Therapy of Diseases of the Circulation.

<sup>13</sup> Ztschr. f. klin. Med., Festschrift, 1890.

<sup>14</sup> Handb. der allg. Path. des Kreislaufes der Ernährung.

he reports the clinical and pathological findings, Virchow<sup>15</sup> thought that the hemorrhages were due to a deficiency in vascular development. Litten holds that if the disturbance be a vascular one, and takes place during foetal development, it may do so in one of two ways—"either in a greater or less development of the connective-tissue germ, or because individual portions of this structure suffer particularly. Of special importance is the fact that it is the maternal element which transmits the disease without being itself necessarily involved, this property being an inherent function of the maternal body and much more marked in the feminine descent than in the masculine. This faculty can exist only in the parablasic tissue and especially in the vascular system which arises from it. Consequently it is very likely that the parablasic of all the tissues of the organism is most influenced by the mother, being less subject to paternal impressions than any of the other constituents."

**PATHOLOGICAL ANATOMY.** It is noteworthy that up to the present time experienced pathologists have not been able to agree upon any pathological findings as characteristic of hemophilia. At autopsy on patients dead from the hemorrhages marked anemia and a waxy appearance of the skin are usually noted. The internal organs contain very little blood and the fluid in the vessels is watery. W. Koch states that some observers have invariably noted an enlargement of the spleen—an observation by no means always verified by others—and believes this enlargement to be significant of the infectious nature of hemophilia. The blood-vessels of the skin are extremely superficial, the larger vessels, particularly the aorta and its main branches, are unusually narrow, the walls thin and elastic. Although this is true generally of the whole arterial system, the capillary vessels show no change. The intima is thin and transparent, the endothelial cells are enlarged, the nuclei swollen, and granular deposits are noted in the protoplasm. In some cases, but by no means in all, fatty degeneration of the intima, together with slight sclerosis, has been demonstrated. The arteries and veins show no large ruptures, the bleeding having evidently occurred from the capillaries. Virchow called particular attention to the persistence of the thymus gland in his case.

König,<sup>16</sup> in 1892, was the first observer to give a graphic description of the pathological findings in the joints. He divides such joints into three classes. To the first belong the cases in which there has been but one hemorrhage and the blood has been rapidly absorbed, leaving no trace except some discoloration of the capsule and synovial membrane. In the second class he places those cases in which repeated hemorrhages have induced thickening and discoloration of the capsule, the cartilage having lost

<sup>15</sup> Deutsch. Klinik., 1859, No. 23.

<sup>16</sup> Volkmann's Samml. Klin. Vorträge, 1892.

its lustre and showing areas of softening. Blood coagula showing connective-tissue changes are found in layers upon the synovial membrane and cartilaginous surfaces, from which grow villi more or less luxuriantly. In the third class he puts those cases in which adhesions have formed between the villous growths; the synovial membrane is greatly thickened, the fluid has been absorbed, and there has resulted ankylosis with the limb in a flexed position.

**SYMPTOMS.** The symptom which first attracts the physician's attention in the majority of instances is an abnormal hemorrhage after some very slight injury, accidental or operative. Among the latter may be mentioned circumcision, the extraction of a tooth, perforation of the lobe of the ear, adenoid or tonsillar operations, or, in fact, any of the numerous minor surgical procedures. Among the spontaneous hemorrhages most frequently met with are epistaxis, bleeding from the gums, intestinal, pulmonary, gastric, renal, cutaneous, uterine hemorrhages, and bleeding into the joints. The hemorrhages are profuse, at times uncontrollable, and terminate in syncope or in death. Hematomas are found occurring upon any exposed part. Prolonged pressure in the sitting or lying posture has been known to produce large hematomas, or these may follow the slightest external violence, such as anyone is apt to incur while pursuing the usual avocations of life. These tumors usually resemble abscesses, and are extremely painful.

About the joint symptoms much has been written and numerous cases have been reported. According to König, in the first stage the condition is apt to be mistaken for acute articular rheumatism or synovitis. In the second stage the appearance is that of a tuberculous joint. In the third stage atrophy, ankylosis, flexion, and possibly subluxation may occur.

Senator,<sup>17</sup> in 1891, reported a case of bleeding from the kidney, and was the first to draw attention to hemophilia as an etiological factor in hematuria. Klemperer<sup>18</sup> and others<sup>19</sup> have reported similar cases. Unquestionably in many of the cases reported the macroscopic and microscopic examinations of the kidneys were not sufficiently thorough to warrant the exclusion of other more common causes. Nevertheless, it is a well-recognized fact that hematuria may be the sole manifestation of hemophilia.

The reports upon the clinical examination of the blood in hemophilia vary slightly as to the differential leukocyte count, but the deviation from normal is scarcely noteworthy. For instance, after examining the blood in three cases, Sahli found that there was a slight relative as well as an actual decrease in the polymorphonuclear leukocytes with a relative increase in the lymphocytes, the total leukocyte count being only slightly decreased or even normal. In two cases the blood platelets gave a low count, although

<sup>17</sup> Berl. klin. Woch., 1891, No. 1.

<sup>19</sup> Volkmann's Samml. Klin. Vorträge, No. 203.

<sup>18</sup> Deutsch. med. Woch., 1897.



not abnormally so. In one case the alkalinity of the blood was not altered. The fibrin was normal in amount. In fact, it may be said that the microscope does not show a sufficient degree of abnormality in the numerical relationship between the corpuscular elements to account for the dyscrasia.

But whereas the morphology of the blood affords us no clue, on the other hand, we know that hemophilic blood has a prolonged coagulation time. In order to make clearer what I shall have to say on this point, let me for a moment revert to the coagulation of normal blood.

The coagulation of normal blood has always been a most attractive subject for investigation. The theories adduced from time to time are numerous, but, in the majority of instances, of little value. The one generally accepted at the present time is that the phenomenon is secondary to the formation of a fibrin ferment known as thrombin, the formation being dependent upon the presence of several different factors, namely calcium salts, prothrombin, and a zymoplastic substance. The calcium salts exist in solution in the plasma. The prothrombin may also preëxist in the plasma or may be furnished by the blood plates or leukocytes, or by both. The zymoplastic substance is derived from the cellular elements in the blood, the vessel wall, or the tissues. Delezenne has shown by very interesting experiments upon birds that when the blood is carefully withdrawn through a cannula inserted into an artery, the blood clots very slowly, and if centrifugalized at once the plasma will remain unclotted for days. If, however, while it is being withdrawn the blood comes in contact with the tissues, those about the wound, for instance, it will clot quickly. Thus it seems evident that in the bird the normal clotting of blood depends upon its coming in contact with the cut tissues. Several theories have been advanced to explain why blood does not coagulate within normal vessels. First, it is assumed that since the formed elements, leukocytes, and blood plates do not disintegrate, one of the principal factors in the formation of thrombin is wanting. Injury to the inner coat of the bloodvessel, the introduction of other foreign substances, and of macerated leucocytes will all precipitate coagulation, for by any of these means, through the destruction of tissue or the blood cells themselves, the formation of the prothrombin and the zymoplastic substance is rendered possible.

For the maintenance of the fluidity of the circulating blood Marowitz supposes the existence of an antithrombin body in it or in the endothelial cells of the vessel walls. If this antibody theory were proved to be correct, an overproduction of this substance in hemophilia might be assumed with some amount of plausibility.

Now, so far as hemophilic blood is concerned, practically in

all instances in which proper measures have been employed, a prolonged coagulation time has been observed, although, inasmuch as different observers using different instruments have obtained different times, a statement in minutes is of little value. It is unfortunate, from the standpoint of exactness, that we have not at our disposal a coagulometer of greater precision than those now in use. The one employed in the study of my case was the Boggs modification of the Brodie-Russell instrument, which seems to fill the requirements better than any of the others with which I am familiar.

In taking the coagulation time in a hemophiliac during a hemorrhage, Sahli observed the following points: The blood was not deficient in fibrin; the blood flowing over the clot outside the wound clotted rapidly, probably owing to the fact that it took up the fibrin factors from the clot; during a hemorrhage of any extent the coagulation time of the blood from another part of the body was shorter than for the same individual under ordinary conditions; after the hemorrhage was arrested the coagulation time shortly reverted to what it was under ordinary conditions. This seems to show that the blood in hemophilia reacts in the same manner as does the blood of a normal individual. It has also been noted that the hemorrhage in hemophilia is prolonged not so much because the blood fails to clot on the surface of the wound as because the bleeding continues beneath the clot, and because the latter does not extend into the vessels.

From these observations it seems that normally the clotting of blood depends upon the action of certain zymoplastic substances derived from the vessel walls as well as from the tissues, and that in hemophilia this substance is certainly deficient in both localities and probably markedly so in the vessel walls. The occurrence of subcutaneous, renal, and joint hemorrhages are to be explained by the same lack of chemical substance in the capillary endothelium which allows the blood to permeate more readily. It is possible, of course, that the deficiency lies in the chemical composition of the blood cells themselves or in the blood-making organs, but as we can ascertain no change in the blood by microscopic examination, it does not seem unreasonable to assume that it is in the vessel walls that the trouble lies, and especially as we have an analogous condition normally in the bird. Moreover, hemophilic patients in many instances manifest a marked hemorrhagic tendency from one locality only, which would seem to indicate a condition approximately normal elsewhere in the vascular system.

**PROGNOSIS.** The outlook is unfavorable in most instances. The disease usually manifests itself before the second year and frequently during the first six months. Only in very rare cases has the hemorrhagic tendency been delayed later than the twenty-first

year. Statistics show that about 60 per cent. of these individuals die before the eighth year, and only about 11 per cent. reach maturity. After forty years of age the tendency to hemorrhage diminishes and may entirely disappear.

**TREATMENT.** As a prophylactic measure bleeders should be advised not to marry, although in the case of males of these families, themselves not bleeders, it may be permissible. Nurslings in whom there is a suspicion of hemophilia should be carefully guarded from even slight injuries, and should not be subjected to any operative procedures; even the application of leeches, blisters, and cups is contra-indicated.

Tonics and a liberal diet with good hygienic surroundings seem the best treatment for the dyscrasia. Vegetarianism and other restricted diets avail nothing. So far as we know there are no drugs which exert any marked influence in correcting the condition. All of the so-called styptics—such as ergot, lead acetate, and silver nitrate—have been employed, but without effect. Calcium lactate exerts a beneficial effect, but only for a short while, after which, in spite of its continued use, the coagulation time again lengthens. Consequently, as soon as the time begins to lengthen the quantity given must be greatly increased, or the drug may be discontinued entirely for a few days, after which its administration will again shorten the period. This point is well demonstrated in the case that I have to report.

The best results in local hemorrhages are obtained from the employment of sterilized gelatin or adrenalin compresses or simple pressure. Sterilized solutions of gelatin injected subcutaneously have also proved efficacious. During pregnancy in hemophilic women any indication of hemorrhage would warrant the induction of artificial labor. If the patient will not consent to this radical procedure, general tonic treatment and the administration of calcium lactate a day or so before the expected confinement will probably give the best results.

Hemophilic joints should be treated with pressure and afforded absolute rest. If the hemorrhage produces great tension, paracentesis followed by the injection into the joint cavity of a solution of adrenalin chloride is advised. This, however, should be the extent of the operative interference. Cases are on record in which hemophilic joints have been opened with fatal hemorrhage resulting, the condition having been mistaken for tuberculosis.

Massage is advised by Gocht, to be cautiously begun a few days after the development of the effusion, not over the joint itself, but over parts slightly distant. This procedure has for its object not only stimulation, but also prevention of the muscular atrophy so frequently seen. When the condition has reached the stage at which there is much thickening of the capsule of the joint, massage with very gentle passive motion is indicated. Force is

contra-indicated in all joint complications in cases of hemophilia. For subluxation suitable braces are to be employed. Hoffa gives very minute instructions as to the management of these cases.

The treatment of the hematuria is extremely unsatisfactory. The ordinary styptics have little or no effect. If general hygienic and tonic treatment is without avail and the patient's condition is going from bad to worse, nephrotomy has been advised and performed in some cases with curative results. Primary nephrectomy is not indicated. Harris<sup>20</sup> reports two cases of so-called essential renal hematuria, and has collected sixteen similar instances from the literature.

The case which I have to report is as follows: D. J. B., aged forty years, a native of the United States, unmarried, a freight conductor. The mother and father are both living at an advanced age. The father gives a hemophilic history from boyhood until the age of twenty-three years, after which time he seems to have outgrown the tendency. One paternal uncle is similarly afflicted. Two paternal uncles and one paternal aunt are not bleeders. The paternal grandmother was a hemophiliac and died of hemorrhage during confinement, aged thirty-nine years. The father's maternal aunt was not a bleeder, but several of her children were. The patient has one brother who is not a bleeder, and one sister who was a bleeder and died at the age of eight years, but not of hemorrhage. Two brothers have a history of repeated and excessive bleeding from the nose and lips during boyhood. They are now thirty-four and thirty-eight years old, respectively, and seem to have outgrown the tendency. Several of the patient's first cousins are bleeders, although their histories are somewhat indefinite.

As a child the patient had measles, but no other disease, so far as he knows, and, with the exception of a gonorrhœal infection later in life, has had no serious illness. He is not addicted to the use of alcohol or tobacco. When a child he had frequent attacks of epistaxis, the hemorrhage being so severe at times as to cause fainting. These attacks continued to be severe until he was about fifteen years of age; since then they have grown less severe, though only slightly less frequent. He has cut himself on the hands and feet from time to time since early boyhood, but never bled to the fainting point, though there was always difficulty in arresting the hemorrhage. He has never had hematuria or joint manifestations. In 1902 he was operated upon for an ingrowing toenail, and nearly bled to death. It was at this time that he first became aware of his hemophilic inheritance. On August 24, 1907, he had a curious abdominal attack which was diagnosticated as "Henoch's purpura(?)" The attack was associated with general

<sup>20</sup> Phila. Med. Jour., March 19, 1898.

abdominal pain and distention; there was no marked muscle spasm in the right iliac fossa, and no especial point of tenderness. Examination of the blood at this time showed the hemoglobin to be 80 per cent., the leukocytes 9800. The differential count of 276 cells showed: Polymorphonuclears, 71; large mononuclears, 7; small mononuclears, 21; eosinophiles, 0.3; mastzellen, 0.7 per cent. The leukocytes the following day were 10,000. Examination of the abdomen showed purpuric spots over the site at which the ice had been applied. The symptoms abated from this time on; the temperature was never higher than 100.2°, the pulse was 80. The patient was discharged from the hospital September 10, 1907.

The present illness began in the latter part of January with the usual premonitory symptoms of typhoid fever, namely, loss of appetite, progressive weakness, headache, slight fever, some diarrhoea, and vomiting; there was nose-bleeding almost daily. He was taken to the hospital February 2. At this time his temperature ranged about 102.5°, six days later reaching 103.6°. The temperature behaved as in an ordinary case of typhoid, reaching normal February 22, but rose the following day to 100°, about which point it hovered until February 29. The evening temperature did not permanently fall to normal till March 23. The pulse was always good, dicrotic at times, the rate never higher than 110. Rose spots appeared about February 8. A positive Widal reaction was obtained February 15. Nose-bleed occurred once on February 11, 22, and 26, and March 1, 4, and 10. The vomitus contained bloody mucus February 8, which was probably from the nasopharynx. There was no blood in the stools at any time. On February 12 the red blood corpuscles numbered 3,952,000; the hemoglobin on February 12 was 70 per cent., on February 26, 60 per cent.; on March 4, 50 per cent.; March 11, 65 per cent.; May 1, 78 per cent.; May 12, 80 per cent.

The coagulation time when first taken was eighteen minutes, the normal limits with the Boggs instrument being from six to eight minutes. By the administration of calcium lactate the time could be reduced to nearly normal by the end of the third or fourth day, after which the time would begin to lengthen in spite of its use. The drug was therefore administered for three days, or until the time began to lengthen; it was then discontinued until the time reached twelve minutes, when it was again administered. In this way the time was always kept within twelve minutes, and often down to seven or eight minutes. The patient was discharged from the hospital April 2, in good condition. The coagulation time on May 12 was fourteen minutes.

The points of interest in connection with this case are: (1) The inheritance came through the father, who was himself a bleeder; (2) this is the first case, so far as I know, of typhoid fever reported in a bleeder; (3) a case of typhoid fever may be brought to a suc-

cessful termination in a patient so afflicted; (4) no hemorrhages occurred from the intestinal lesions; (5) the successful termination in this instance was probably in a large measure due to the fact that at or about the age of forty the hemorrhagic tendency abated; (6) in this man's case the principal manifestation of the hemorrhagic tendency had been attacks of epistaxis, the only other serious hemorrhage having occurred at the time of the operation upon his toe. Whether the careful administration of calcium lactate is really of substantial benefit can only be determined in the future after trial in a relatively large series of such cases.

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## THE ETIOLOGICAL FACTORS OF COMPRESSED-AIR ILLNESS.

THE GASEOUS CONTENTS OF SUBAQUEOUS TUNNELS; THE OCCURRENCE OF THE DISEASE IN WORKERS.

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AMONG the great engineering feats of the past ten years, perhaps none has been greater than the building of the subaqueous tunnels under the East River, New York City. In this work man has to contend not only with the dangers of ordinary tunnel construction, but also with those of compressed-air illness, or "bends," a disease or condition to which all workers in compressed air are liable. The word "bends" has come into vogue among the workmen because of the supposed characteristic attitude assumed by these sufferers in their efforts to relax the affected muscles and to relieve the pain. These cramps may occur in a group of muscles, such as those of the abdominal wall or of the extremities, and frequently the pains are referred to the joints.

Compressed air is, of course, necessary in subaqueous tunnel construction, for it supports the river bottom, which the work of excavation leaves partly unprotected, and thus prevents the river from flooding the tunnel. The amount of air pressure required varies greatly and is dependent upon the depth of water above the tunnel. The pressure necessary may be roughly estimated at fifteen pounds to every thirty feet of water.

It has been suggested by Snell,<sup>1</sup> E. W. Moir, Leonard Hill,<sup>2</sup> and others that certain gases, when present in compressed air tunnels, may influence the number of cases of "bends." The purpose of this paper is to describe these gases, particularly carbon

<sup>1</sup> Compressed-air Illness, London Magazine, 1896.

<sup>2</sup> The Junior Institute of Engineers, 1907, xviii, 65.

dioxide and carbon monoxide, and also to describe other atmospheric conditions found in subaqueous tunnels and the effect these have in the etiology of compressed-air illness, or "bends." I wish also to demonstrate the prevalence of "bends" among new men, those subjected for the first time to high atmospheric pressures. An analysis is attached of one air sample taken from the right auricle of a man who died of compressed-air illness, which analysis is believed to be one of few, if not the only one of its kind.

Two and one-half years' experience as one of the medical officers on the staff of S. Pearson & Sons, Incorporated, constructors of the Pennsylvania Railroad East River Tunnel, gave me unusual opportunities for observation and study in this line, owing to the magnitude of the work. The observations on air analysis embodied in this article are based on results obtained from daily records of the four tunnels. During the year 1907 a special chart was kept, giving in detail the daily air analyses, the number of men at work, the amount of air pumped into the tunnel, and the air pressures.<sup>3</sup> Estimations were first made of carbon dioxide.

**CARBON DIOXIDE ( $\text{CO}_2$ ).** *Properties.* Carbon dioxide, colorless at ordinary temperatures; slightly acid taste and odor; incombustible and not supporting combustion; heavier than air, specific gravity, 1.529.

*Source.* Normally  $\text{CO}_2$  exists in only the most minute quantities, excepting in pockets of coal (fire-choke); in the vicinity of certain mineral springs or active volcanoes; as a by-product in fermentation, decomposition, and putrefaction of organic matter; and is formed in human or animal respiration, and in blasting.

*Effect on Man.* Carbon dioxide is in no way a poisonous gas. This has been proved by the experiments of Leonard Hill and others. That when present in large quantities in the air we breathe it will cause death, is an undoubted fact; but death is then caused by suffocation, as in drowning, from the absence of oxygen. Authorities differ as to the permissible amount of  $\text{CO}_2$ , but as most tunnel contracts call for air containing not over 0.1 per cent. of  $\text{CO}_2$ , we shall consider this as our standard. This figure is most conservative, in fact, seemingly unnecessarily so.

*Detection of  $\text{CO}_2$  in Air.* The percentage of  $\text{CO}_2$  is most commonly determined with the Palmquist apparatus<sup>4</sup> or by the Hesse method.<sup>5</sup> All the analyses for  $\text{CO}_2$  in the tunnels were made with the Palmquist apparatus. Although this apparatus is not absolutely accurate, the results were made fairly so by checking them with those obtained by Hesse's method.

Normal air contains  $\text{CO}_2$  in very minute quantities. The amount varies, being high in large cities, while in remote country districts

<sup>3</sup> I am greatly indebted to Professor J. Livingston R. Morgan, of Columbia University, for his invaluable assistance and the use of his laboratory during the summer of 1907.

<sup>4</sup> Hempel's Gas Analysis, 1902, p. 363.

<sup>5</sup> Ibid., p. 337.

CO<sub>2</sub> is practically absent. For New York City in the vicinity of the East River tunnels the average amount was 0.0363 per cent. by volume.

*Compressed air* taken directly from compressors contains CO<sub>2</sub> in slightly larger quantities than does normal air, averaging about 0.0423 per cent. by volume. This difference, 0.006 per cent., between compressed and normal air is so minute that it is of no consequence.

*The Source of CO<sub>2</sub> in Compressed-air Tunnels.* In subaqueous tunnels CO<sub>2</sub> might be traced to any or all of the following sources: (1) Decomposition, putrefaction, or fermentation of organic matter. This source of CO<sub>2</sub> contamination was eliminated by comparing the analyses of samples of air taken in the tunnels which were temporarily not being worked, and of samples of the air supplying the tunnels. These proved to be practically the same. (2) Respiration in man consists in inspiring oxygen, nitrogen, and other gases in minute quantities, and in expiring carbon dioxide, nitrogen, oxygen, and an indeterminable amount of foreign matter, which may or may not be noxious. The increased CO<sub>2</sub> in expired air represents a corresponding amount of O<sub>2</sub> lost from inspired air. Therefore, if this air be not constantly changed, CO<sub>2</sub> becomes of immediate importance, and suffocation will rapidly ensue, not from the presence of CO<sub>2</sub>, but from the loss of oxygen. Pettenkofer<sup>6</sup> suggests that carbon dioxide is a good index of the amount of deleterious substances given off by expiration, and as we are not able to determine these substances accurately, we may gauge the purity of the air by the percentage of carbon dioxide present. (3) Blasting will be described more fully under carbon monoxide. It is sufficient for the present to know that carbon dioxide is one of the gases given off. Analysis of a sample of air from a "heading," taken immediately after a blast, showed the CO<sub>2</sub> to be as high as 0.657 per cent. by volume, while ten minutes later a sample taken in the same place showed only 0.07 per cent. by volume, and half an hour after a blast the air contained the same amount of this gas as it did before. Therefore, the presence of carbon dioxide in the air of the tunnels is due practically to human respiration.

Air samples were taken daily in the tunnels, and in order that these analyses might be general, the samples were collected at several points, namely, in front of and behind the "shield," in the "pockets" of the shield, and at four or five places throughout the length of the tube.

The following figures are compiled from several thousand CO<sub>2</sub> readings, taken during the year 1907, of samples of air from behind the "shield" where a number of men were always at work, and they therefore show a fair maximum average for the four tunnels: Maximum, 0.1 per cent. by volume; minimum, 0.045 per cent. by volume;

<sup>6</sup> Hempel's Gas Analysis, 1902, p. 336.



average, 0.07 per cent. by volume. Since in our tunnels the amount of carbon dioxide in the air seldom if ever exceeded 0.1 per cent. by volume, it is my opinion that this gas has not the slightest influence on compressed-air illness. In substantiation of this view, it was found that on the charts of the four tunnels in which the daily  $\text{CO}_2$  fluctuation and the number of cases of "bends" were recorded, the amount of  $\text{CO}_2$  bore no relation to the number of cases of illness.

**CARBON MONOXIDE (CO).** Carbon monoxide (CO) is a colorless, odorless, combustible gas, lighter than air; specific gravity 0.967. This gas, aside from being explosive, combines readily with hemoglobin, forming a most stable compound, and thus preventing oxygen from being carried to the tissues, and eventually causing death by suffocation. For these reasons CO has always been considered one of the most dangerous of gases.

In taking up the work of determining small quantities of CO in high-pressure tunnels, some simple method was the first consideration, and an equally simple, effective, and practical method for the collection and preservation of the air sample. An air cylinder suggested by Professor Morgan, of Columbia University, was made, and proved to be most satisfactory. Samples collected up to thirty pounds gauge pressure and over were kept for more than a month without loss of pressure. The cylinders were made of copper, and caps of the same material were screwed in place and brazed. At either end were compression cocks fitted with leather gaskets. Of the two, one was so arranged that a pressure gauge might be attached, the other was drawn out and corrugated for rubber tubing which connected with the CO apparatus. The capacity of each cylinder was accurately determined to be from 1035 to 1045 c.c.

A study of the writings on this subject showed that very little had been done in determining small quantities of carbon monoxide. The ordinary method of quantitative CO determination was by the use of some apparatus such as Orsat's,<sup>7</sup> the principle of which is absorption of this gas by cuprous chloride. This apparatus is very simple to manipulate, and gives CO readings within 1 per cent. It is generally used in determining the amount of CO in flue and illuminating gas, but it is of no value in determining minute quantities. The other, a more delicate but purely qualitative method, was the spectroscopic examination of the blood for carbon monoxide hemoglobin. Kinnicutt and Sanford<sup>8</sup> devised a very accurate method of determining small quantities of CO, and a simple modification of this by Professor Morgan and myself<sup>9</sup> is the one upon which all these determinations are based.

The presence of CO in the East River tunnels might be traced

<sup>7</sup> Hempel's Gas Analysis, 1902, p. 257.

<sup>8</sup> Journal of the American Chemical Soc., 1900, xxii, 14.

<sup>9</sup> Ibid., 1907, xxix, 1589.

to any or all of the three following sources: (1) A large gas tank immediately adjoining the works. A sample of air taken in this neighborhood showed no CO. (2) Flue gas. None was found at "intake flues" for compressors. (3) Blasting. This was carried on very extensively during the rock boring period of the tunnel construction, and to this we must trace our supply of CO.

In the blasting the explosive used was dynamite, the active principle of which is nitroglycerin. Dynamite in exploding liberates certain gases. Under the most favorable circumstances the gases liberated are  $\text{CO}_2$ ,  $\text{N}_2$ , and  $\text{O}_2$ . When the dynamite is of inferior grade, however, when it is damp, or when for any other reason there is incomplete combustion, the gases given off besides those already named are CO, NO,  $\text{CH}_4$ ,  $\text{H}_2$ , and  $\text{H}_2\text{S}$ , in amounts dependent upon the amount of incomplete combustion. The amount of CO given off in explosions of dynamite varies greatly. It may be in very small percentages or as high as 36 per cent., or even higher.<sup>10</sup>

Before the quantitative method of CO determination was perfected, spectroscopic examinations were made on two blood samples through which tunnel air had been passed. These are inserted, since I feel they help to prove that CO in small quantities is not to be detected by spectroscopic examination.

The two following spectroscopic blood analyses were made by Dr. T. W. Hastings at the Cornell University Medical College, New York City.

*First Report:* Dynamite used, amount 11 pounds 13 ounces. Absorption solution: 5 c.c. human blood, fibrin extracted; 20 c.c. distilled water; 1 gram ammonium oxalate. Through this solution, air in No. 1 tunnel "centre pocket," one minute after firing, was allowed to circulate for ten minutes.

*"Spectroscopic analysis.* (1) Blood exposed to air in heading after blast. Dark brownish red in color. Spectrum of methemoglobin; reduces with ammonium sulphide. No trace of carbon monoxide hemoglobin. (2) Control solution bright red in color. Spectrum of oxyhemoglobin; reduces with ammonium sulphide. Normal blood."

*Second Report.* Dynamite; very heavy blast, amount not known. Through 500 c.c. of oxalated bullock's blood, 4 liters of tunnel air, taken in heading and directly after blasting, was allowed to circulate. The air sample was allowed to circulate very slowly through the blood solution, the time consumed being one hour and forty-five minutes.

*"Spectroscopic analysis* (August 14, 1907). Oxyhemoglobin (by scale); reduces to reduced hemoglobin. Carbon monoxide hemoglobin not detected."

<sup>10</sup> A more complete description of gases given off in explosions may be found in Foster and Haldane's work, *The Investigation of Mine Air*, 1905, pp. 133, 134.

In this last blood examination it will be seen that tunnel air at its maximum CO saturation was allowed to circulate for one hour and forty-five minutes through the blood solution. This is a most abnormal condition, and one to which no tunnel worker is subjected, as will be demonstrated later, yet, as shown in the above report, no CO hemoglobin was found.

The following CO determinations are selected from the analyses made (during the year 1907) in the four tunnels. They show what small percentages really were present in those tunnels; but in land tunnels with poor ventilation and heavy blasting, it will readily be seen, as explained later, how rapidly CO might accumulate, in percentages high enough to be of grave concern.

1. Dynamite, 6 pounds 7 ounces, fifteen minutes after blasting: CO=0.01 per cent by volume.

2. Very small blast, ten minutes after firing: CO=0.0075 per cent. by volume.

3. Dynamite, 41 pounds 13 ounces, immediately after firing: CO=0.031 per cent. by volume.

4. Dynamite, 45 pounds 1 ounce, immediately after firing: CO=0.0423 per cent. by volume.

5. Second sample same as No. 4, but one minute after high pressure air line had been opened to clear heading: CO=0.02 per cent. by volume.

6. Sample taken ten minutes after firing of a very heavy blast, the amount of dynamite not known: first sample, CO=0.045 per cent. by volume; second sample, CO=0.05 per cent. by volume.

7. Dynamite, 5 pounds 15 ounces, immediately after blasting in "sump"—pumping chamber built in rock between tunnels—very confined: CO=0.015 per cent. by volume.

All these samples, with the exception of No. 7, were taken as near as possible to the "heading" where the blasting had taken place, and represent the highest percentage of CO obtainable.

A very fair average of the amount of CO present during the blasting period was about 0.025 per cent. by volume. This naturally varied according to the amount of dynamite used, its quality, and the completeness of its combustion. The percentage given above was not an average percentage throughout the tunnel, but that found in the heading after blasting. As these samples were taken immediately or very shortly after blasting, they represent the very worst atmospheric conditions. Until the "heading" is cleared by means of either the "blow pipe," a large eight to twelve inch suction pipe communicating with the normal air in the shaft, or the high pressure "air line," which clears the heading by blowing back into the tunnel all gases and smoke, the men do not resume their work. Both methods of "clearing the heading" are very effective, for in samples taken one hour after blasting it was impossible to determine CO in quantities over 0.002 per cent., the minimum detectible by our

method. The practice of clearing the "heading" in poorly ventilated rock tunnels by blowing the smoke and gases back into the tunnel, although a rapid method, can hardly be recommended for even the small amounts of CO given off by each blast will in time accumulate in sufficient quantities to be toxic.

Vogel,<sup>11</sup> who first described the spectrum of CO-hemoglobin, and, later, Gustav Walffhugel<sup>12</sup> state that in their opinion "quantities less than 0.25 per cent. of CO may be disregarded from a hygienic standpoint." (This figure, in the light of more recent investigations, is shown to be much too high.) Harrington<sup>13</sup> says that CO in quantities less than 0.25 per cent. will cause poisoning, and that "1 per cent. is rapidly fatal to animal life." Foster and Haldane<sup>14</sup> say, "Anything above 0.15 per cent. must be regarded as distinctly dangerous, and probably anything over 0.03 per cent. (CO) would in time produce symptoms distinctly felt on exertion." C. H. Wolf<sup>15</sup> claims to have demonstrated CO-hemoglobin in atmospheric air containing not over 0.03 per cent. CO. In the spectroscopic report made by Dr. Hastings the amount of CO must have been fully 0.03 per cent., but no CO-hemoglobin was demonstrated.

As the maximum amount of CO in our tunnels never exceeded 0.045 per cent., and as this quantity was present for only a very few minutes immediately following the firing of a blast, one could hardly expect this to influence in any way the number of cases of bends, and this was further substantiated by the complete absence of any clinical signs of CO poisoning. As further proof it may be added that in a chart kept of the same tunnel, first, when blasting was being carried on very extensively, and second, when there was no blasting, the air pressures and the number of men at work being the same, the cases of bends were practically equal.

Certain of the men did, however, complain at times of headache after a very heavy blast. These were always men who went ahead with the high pressure "air line" to clear the heading, or who were there for some other purpose. As these headaches were never accompanied by any other symptoms of CO poisoning, such as dizziness, shortness of breath, or muscular weakness, and as the headache disappeared when the heading cleared up, I do not regard them as a sign of CO poisoning.

**OTHER GASES FOUND IN TUNNELS.** At various times during the year 1907 samples of tunnel air were analyzed to determine if possible the presence of any one or more of the following gases in quantities sufficient to be dangerous: Methane ( $\text{CH}_4$ ), sulphuretted hydrogen ( $\text{H}_2\text{S}$ ), and nitric oxide ( $\text{NO}$ ). I used a Hempel's gas analysis apparatus<sup>16</sup> which was especially constructed to read small

<sup>11</sup> Hempel's Gas Analysis, 1902, p. 217.

<sup>13</sup> Principles of Hygiene, p. 218.

<sup>15</sup> Hempel's Gas Analysis, 1902, p. 222.

<sup>12</sup> Ibid., p. 217.

<sup>14</sup> Investigation of Mine Gas, 1905, p. 133.

<sup>16</sup> Hempel's Gas Analysis, 1902, p. 59.

percentages of gas, the burette scale reading to  $\frac{1}{100}$  of a cubic centimeter. The results of this work were mostly negative, for methane was never found, while nitric oxide and sulphuretted hydrogen were present only occasionally and in the most minute quantities.

**WASTE MATTER, AQUEOUS VAPORS, AND TEMPERATURE IN TUNNELS.** The amount of waste matters such as oil from compressors or any other organic or inorganic matter that might be forced through the air feed pipes, was relatively small, as was proved by the amount of deposit on the gauze screens at the mouth of the feed pipes.

The amount of aqueous vapor in the tunnels was very high, generally to complete saturation. Occasionally this would vary for short periods, and was dependent upon the amount of air leakage. Hygrometers left in tunnels never registered below 90° of saturation.

The temperature in the tunnels varied with the amount of air pumped in to maintain the required pressure, its length, and the time of year, averaging about 75°.

**VENTILATION.** In order to maintain perfect ventilation it is generally conceded that from 2000 to 3000 cubic feet of fresh air per man per hour is more than sufficient. In the East River tunnels this amount was always exceeded, as the average amount of fresh air per hour was about 231,000 cubic feet, or about 7699 cubic feet per man per hour.

In connection with these determinations of the gaseous contents of the tunnel air, it is of interest to note that of a sample of air obtained from the right side of the heart of a man who died of "bends." The sample was collected at autopsy about five hours after death, by the following method: The pericardial sac was filled with water and an aspirating needle, which was connected with a specially devised air collector, was introduced under water into the right auricle, great care having previously been taken to displace by water all air in the collector tubing and needle. About 5 c.c. of gas was collected—much more could have been obtained if desired; and a quantitative analysis was then made.

The following report was made by Floyd G. Metzger, Ph.D., at Columbia University.

"New York, November 20, 1907. Certificate of Analysis. The sample of gas from S. Pearson & Sons, Incorporated, marked "Sample taken from right side of heart," submitted to me for examination, contains: Nitrogen, 80 per cent.; carbon dioxide, 20 per cent.; oxygen, immeasurable quantity."

Analysis of gases from normal venous blood:<sup>17</sup> From 100 volumes may be obtained: Nitrogen, 1 to 2 per cent.; carbon dioxide, 46 per cent.; oxygen, 8 to 12 per cent.

In comparing the two analyses one is naturally struck by the great difference in the two samples. This may be explained as follows: The nitrogen which goes into solution under pressure remains unchanged, and is given off with carbon dioxide in the venous circulation as bubbles when normal atmospheric pressure is reached, and collects in large quantities in the right heart. The absence of oxygen is probably due to its having combined with the body tissues either before or shortly after death.

In a fatal case of "bends," if the man has been recompressed several times and does not die until twelve hours after the beginning of the attack, or if the autopsy is not performed within twelve to twenty-four hours after death, air in any considerable quantities is, as a general rule, seldom found; but when a man dies shortly after coming out of pressure, the right heart is almost invariably greatly distended with gas, and the whole venous system contains many bubbles.

**FREQUENCY OF THE DISEASE AMONG NEW WORKERS.** Having considered the insignificance of the variation of the individual gases as a causative factor of "bends," I now take up the frequency of this disease among new workers.

*Examining Men for Tunnel Work.* Before going to work all men were given a rigid physical examination. In the case of green and new men, besides this examination they were sent in charge of a competent man for a test of one and one-half hours in the tunnel. On coming out, they were brought back to the doctor's office and reexamined. If any changes were noted in their condition, they were excluded from tunnel work. Of the many thousands of men who went into the tunnels for the hour and a half test only one was known to have had the "bends."

*Length of Shifts of New Men.* After a new man had passed for tunnel work, his first day consisted of part of one shift, instead of one whole shift; that is, six hours on an eight-hour shift, four and a half hours on a six-hour shift.

*Prevalence of "Bends" Among New Workers.* It has been stated by McLeod<sup>18</sup> and others that old compressed-air tunnel workers are just as susceptible to "bends" as are the new men. This in our experience was far from being the case, as will be shown later, in the results collected from charts of the four tunnels kept during the year 1907, at the New York City end. On these charts a distinction is made between absolutely new compressed-air workers and those who for some reason claimed previous experience. In the latter class a large percentage really were new workers in high pressures, for some had been away from this work for a long time; others had worked in but very low pressures in caisson work; while undoubtedly many others had never been near a pressure tunnel.

<sup>18</sup> Assoc. of Engineering Soc., 1907, xxxix, 301.

*The Amount of Air Pressure in East River Tunnels.* During the year 1907 the air pressure in the tunnels varied, ranging from 26 pounds to 34 pounds above normal atmospheric pressure; a fair average during the year was about 29 pounds.

*The Percentage of Compressed-air Illness Among Different Workers.* The following table gives the number of men classified as: *Green men*, namely, those new to compressed-air work, *new men*, namely, those new in this tunnel; and *old men* (approximate), who entered for work in the New York side during 1907; also the number of cases of "bends" in each group and the percentage.

The numbers of cases of "bends" given for "green" and "new" men were collected from the histories of those attacked at the end of their first or second day's work in the tunnel. Of this number, the majority were affected at the end of the first day.

	No.	Cases of "bends."	Per- centage.
Green men (new to this work) . . . . .	308	48	15.5
New men (new to this tunnel) . . . . .	641	60	9.4
Old men (days) . . . . .	150,664	657	0.43

In our experience it was found that compressed-air illness varied with the pressure—the higher the pressure the more susceptible the men were to the disease. Particularly was this true of new workers, for at 27 pounds and under, comparatively few men were affected, while at 30 pounds and over a large percentage was attacked.

In endeavoring to explain the susceptibility of new men to high pressures, one must consider the abnormal conditions under which these men work. Man has become accustomed to live and work in a certain atmospheric pressure, normally about 15 pounds to the square inch. In compressed-air tunnels he lives and works in an atmospheric pressure of from 35 pounds to 45 pounds and over to the square inch, and until he has adjusted himself to his new environment, he is susceptible to compressed-air illness. That a man's body does adjust itself to this environment seems amply proved by the vast number of subaqueous tunnel builders alive today.

In closing, it may be mentioned that men working in low pressure, that is, those ranging from 15 to 20 pounds, and in shifts not over eight hours in length, are not at all liable to "bends." In fact, in our experience a case of "bends" at these pressures was extremely rare.

**CONCLUSIONS.** In this article an endeavor has been made to prove the following:

1. In subaqueous tunnels the loss of air by leakage is sufficient to maintain perfect ventilation, and, therefore, carbon dioxide, carbon monoxide, and other gases do not accumulate in sufficient

quantities to be considered as a possible etiological factor in the causation of compressed air illness.

2. The direct cause of compressed air illness is the presence of air bubbles in the circulation; these gas bubbles consist of nitrogen, carbon dioxide, and oxygen, of which nitrogen is in excess, for the reason that this gas is the chief constituent of the atmosphere, and also does not combine with any of the body tissues.

3. New workers are most susceptible to this disease until the body accommodates itself to this entirely abnormal condition of high air pressure; and, therefore, it is of the utmost importance that only young, healthy men should be allowed to do this work. New workers should, when feasible, be started in low pressures, from which in the course of four or five days they may graduate to become, as they are called, "high pressure men."

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## MYATONIA CONGENITA, OF OPPENHEIM.

### OR CONGENITAL ATONIC PSEUDOPARALYSIS.

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THE condition described as myatonia congenita by Oppenheim, of Berlin, and sometimes called Oppenheim's disease, seems to have found but little recognition in America, as no mention is made of it in recent text-books, be they of neurology, pediatrics, or internal medicine. And yet the first autopsy case was published by an American, Spiller, of Philadelphia, and since then a considerable European literature has sprung up around the subject. Possibly one reason for this apparent neglect is the similarity of Oppenheim's appellation to that of myotonia congenita, or Thomsen's disease, which appears invariably to be thought of when the name is mentioned. I may add that there is yet another condition unfortunately similarly named, "Myotonie der Neugeborenen und Säuglinge," of Hochsinger.<sup>1</sup> To avoid confusion, therefore, I have applied the name congenital hypotonic or atonic pseudo-paralysis to the disease; this is merely a descriptive cognomen, the pathology being still unsettled.

Before proceeding farther, I shall give the history of three cases (from Oppenheim's Polyclinic at Berlin); the third<sup>2</sup> is somewhat

<sup>1</sup> Krämpfe bei Kindern, Die Deutsche Klinik, vol. vii.

<sup>2</sup> For permission to publish these case reports I am indebted to Professor Oppenheim.



exceptional, and is here published for the first time; the first and second are typical and have been already reported by me.<sup>3</sup>

CASE I.—Emma R., aged three and one-half years. The mother brought the child to the clinic because it could not use its legs since birth. The upper extremities have always been normal. The child is, in regard to its intelligence, normally developed. Pregnancy and parturition were nowise complicated. Labor was not prolonged. There was no cyanosis at birth, nor any injury nor acute disease since. Examination shows complete hypotonicity of the lower extremities. Neither patellar nor Achilles reflexes can be elicited. The child can flex the foot upon the leg, but only with much reduced strength. The upper extremities, though they can be voluntarily moved in all directions, also show some weakness. Only if supported on both sides can the child propel itself forward, and this with much effort. Because of the child's excitement, the electrical examination was not complete; but this much was ascertained, that the cruralis and obturator on the left side gave no reaction at all, while the peroneus showed decreased electric irritability.

CASE II.—W. J., aged four months. This patient was referred to us from the clinic of Professor Hoffa. The child was born at the normal time; the parturition was easy. There is no history of any trauma. The mother felt foetal movements until just shortly before labor. The child was at the breast for five weeks, and was then artificially fed. No gastro-intestinal disturbances have occurred. Looks well nourished; the size is that of a normal infant of this age. With the exception of the fingers and toes, the child may have been paralyzed since birth. It moans while being examined and lies motionless. The skin on the legs appears in places slightly mottled and cold to the touch. The patellar reflexes are absent. Complete atony is present. The extremities, being placed in most uncomfortable positions, are left so. Even when irritated by pain (pinch or pin prick) no movement is made, or only very slight ones in the feet and toes, and very gradually. In the arms a similar atony exists. The forearm is bent, the hand pronated, and the fingers held together (slight secondary contraction). Only in the fingers does one see some slow active movements. Even upon pricking with the needle no movement is made. With inspiration the diaphragm is drawn well down, the ribs to which it is attached being thereby somewhat drawn in. The abdomen is distended, the umbilicus pouting. The abdominal reflex is absent. The child cannot as yet sit up. It can move its head. The movements of the eyes are normal. The large fontanelle is closed. The neck is short, but apparently there is no pathological condition here. The cervical spine shows lordosis

<sup>3</sup> Zur Differentialdiagnose der Poliomyelitis anterior acuta, Karger, Berlin, 1908.

and lies deep. The dorsal spine is somewhat kyphoscoliotic (doubtlessly congenital). Needle pricks are normally felt in the face. The electrical reaction shows a quantitative but no qualitative change in the muscles of the thighs. In using a strong galvanic current the muscles contract with rapidity.

CASE III.—A. A., aged one and one-half years, female. There is nothing of hereditary significance. The mother is said to have felt strong foetal movements. Labor was normal at term, there was no instrumentation, and the child showed no asphyxia. In the fifth or sixth month the mother noticed that the child could not hold its head up, nor sit up (which it had already attempted). Then gradually the present condition developed. On further questioning it appears that the child never really kicked nor used its feet as the normal infant does. It therefore becomes doubtful whether or not the condition was entirely congenital or acquired. At any rate, it seems that an exacerbation occurred in the fifth or sixth month. The child looks well nourished, and has a healthy color. It appears intelligent, notices all that is being said or done. At present it cannot stand, or sit, or hold its head up. In the beginning it sucked well; this has become difficult. There is severe constipation. The head is normally shaped. There is no craniotabes; the fontanelle is closed. The child repeats single words normally. Hearing is good. The pupils react promptly; ophthalmoscopically normal. There is a tendency to convergent strabismus. Movements of the facial muscles are normal. Breathing is somewhat snoring. When let go, the child just doubles up as if made of rubber. The head is balanced with much difficulty, and the slightest movement sends it over. Both upper extremities are flabby, lacking all tone, though some movements are to be seen here. The child should be able to raise the arms somewhat in the shoulder. At present, when raised, both limbs again fall back upon the table. In the hands and fingers constant movements are seen, which at first appear athetoid in character, but are certainly more in the nature of play impulses. No reflexes can be obtained. The legs are absolutely atonic. The patellar and Achilles reflexes are absent. A real plantar reflex is not obtainable, only an occasional contraction or extension if this region is irritated. The toe reflex (Bechterew-Mendel) on the left side is mostly dorsal; on the right also, but not constant. The limbs lie extended in extreme outward rotation. Passively lifted they fall back as if lifeless. Active movements are to be seen in the toes. If placed in a very awkward and uncomfortable position, the legs are brought out of this only slowly, and chiefly by movements of the feet. Even when stuck with a needle no lively movement or reflex can be obtained. Occasionally one notices a contraction of the quadriceps. The abdomen is distended. There

is no abdominal reflex. The muscles are hypotonic. The diaphragm appears to act normally. The atony of the muscles of the back is especially intense, but so also is that of the hip- and knee-joints. There is considerable adiposis, which masks the atrophy that may be present. There is divergence of the lower part of the thorax. Sensation appears to be normal. The thyroid cannot be distinctly palpated. The percussion note over the sternum is strikingly short. Electrical examination shows marked lessening of irritability for both currents in the lower extremities, less so in the upper. The facial muscles react normally. There is no reaction of degeneration anywhere.

Studying these cases, we find certain points in common—a rather extensive apparently flaccid paralysis, with absence of patellar and Achilles reflexes. In one there is vasomotor disturbance, in another slight atrophy, masked, however, by adiposis. Viewed thus far these cases might be taken for anteropoliomyelitis. A little closer analysis, however, will bring out certain interesting facts—namely, that Cases I and II with certainty, and Case III quite probably, date from birth, or, in other words, are congenital. Now, congenital cases of anteropoliomyelitis appear not to exist. The one case cited in the literature<sup>4</sup> belongs possibly to the group of cases I mean to describe<sup>5</sup> and has nothing to do with poliomyelitis, as two other children of the family were similarly afflicted (familial intra-uterine poliomyelitis!), and the paralysis was progressive—increased instead of decreasing, as is the rule in anteropoliomyelitis. Furthermore, there is no really degenerative atrophy present with reactions of degeneration. The paralysis which is extensive, especially in Cases II and III, has not gradually confined itself to an area smaller in extent than that which was at first affected, as is almost invariably the case in anteropoliomyelitis. Finally, on careful examination, one sees that some movements are present in the affected muscles, that we are not really dealing with genuine paralysis, but with an extreme condition of muscular atony. These muscles feel soft and doughy, and, excepting in the one case, not cold to the touch. We have, therefore, before us a symptom complex which deviates widely from that found in infantile spinal paralysis.

In 1900 Oppenheim<sup>6</sup> described a condition of general or localized atony of the muscles, concerning which he said he had found nothing

<sup>4</sup> A. Sevestre, *Ref. Neurol. Zentral.*, November 9, 1900, S. 904 (Paralysie flasque les quatre membres et des muscles du tronc, etc., *Bull. de la Société de pédiatrie de Paris*, Fév.-Mars, 1899).

<sup>5</sup> H. Oppenheim, *Lehrbuch*, p. 224.

<sup>6</sup> Ueber allgemeine und lokalisierte Atonie der Musculatur (Myatonia) im frühem Kindesalter, *Monatsschrift f. Psychiatrie u. Neurologie*, 1900, Band viii, Heft 3, p. 232. Ueber einen Fall von Myatonia congenita, *Berl. klin. Woch.*, March 7, 1904, No. 10, p. 255; also *Berliner med. Gesellschaft, Sitzung*, February 24, 1904.

in the literature. These cases occurred within the first two years of childhood, and showed as especially characteristic a hypotony or even atony of the muscles combined with partial or complete loss of the tendon reflexes. The limbs, particularly the lower, were at times so flaccid that they could be shaken like flails. There was in all cases an impairment of active motion. When the condition was extreme, the limbs lay perfectly still, and it appeared as if complete paralysis obtained. But on more careful observation, one could note occasional contractions in various muscles, which, however, were feeble, and lacked sufficient energy to give locomotive effect. Less involved cases showed only hypotony and a marked weakness. In one case the muscles of the trunk and neck were affected, besides those of the limbs, so that the infant of eight months could neither sit up nor support its head. Even in so generalized a condition, however, the muscles of the eyes, tongue, and throat were unaffected, as also the diaphragm. The intercostals, on the other hand, appeared to be involved. The muscle felt flaccid and soft, and appeared to be thin, though one could scarcely apply the term atrophic. Electrical examination showed in the severer cases a considerable quantitative, though never qualitative, alteration, up to even complete disappearance of reaction. In mild cases the reaction was normal. In but one case tardy contraction, and this only in portions of the muscle, was observed. No abnormalities, so far as it is possible to judge in such young infants, were discoverable in the sphere of intelligence, sensory system, or special senses. The malady always appeared to be congenital. In its typical form it seems to be the antithesis of Little's disease.

Oppenheim thought the pathological factor of this condition was to be sought, not in the central nervous, but in the muscular system, which was probably retarded in its development—for not only was he able now and again to observe partial or complete return to the normal within the course of time, but because he never had occasion to notice this condition in older children. He did not think it had aught in common with progressive muscular dystrophy. He did not entirely exclude the possibility of disease in the anterior horn cells prompting the developmental inhibition of the muscles.

Shortly after other cases began to appear in the literature, two of Berti's,<sup>7</sup> and then one, the first with necropsy, of W. G. Spiller's.<sup>8</sup> This last case was a child of twenty-two months. The head, trunk,

<sup>7</sup> Contribuzione all' Atonia muscolare congenita di Oppenheim (Terza adunanza della sezione Emiliana della Società Italiana di pediatria, 4 Dez. 1904, in *Pediatria*, February, 1905, p. 134).

<sup>8</sup> General or Localized Hypotonia of the Muscles in Childhood, *Univ. Penna. Med. Bull.*, 1905, xvii, No. 11. See also Bernhardt, *Neurologisches Zentral.*, 1907, No. 1. Spiller, *Ebenda*, No. 11.

and extremities were affected. There was very great hypotonicity of all the limbs, especially the lower (which could be flexed so as to bring the thighs in close contact with the trunk, and the feet easily behind the head). The child could not stand, sit unaided, hold up its head, or hold anything in its hand. It had always been constipated. The faradic electrical response was retained. Besides convergent squint,<sup>9</sup> certain abnormal conditions of the internal eye obtained, which, as they have nothing to do with the general condition, need not further be considered here. The child died during fever of unknown cause. The autopsy, made twenty-four hours post mortem, showed absence of postmortem rigidity and a hypotonicity of the limbs as great as that during life. The muscles were flabby. Section of the calf showed fat 6 mm. in thickness, with very little muscle, and this paler than normal. There was hardly any muscle in the sole of the left foot. The subcutaneous fat over the triceps measured 3 mm. The brain weighed 980 grams; the dura was adherent. The spinal cord and brain were well developed; the anterior and posterior roots normal. Microscopic examination of the brain, cord, nerves, and muscles (made by Professor Spiller personally) showed normal cells in the anterior horns of the cervical and lumbar regions (thionin stain), and a normal condition of the nerve roots. No spinal meningitis was present. There was no degeneration in the pyramidal tracts. Marchi sections showed no degeneration. The optic nerves were normal (Weigert and Marchi). The nerve cells of the paracentral lobules appeared normal, but in the section Betz's cells were not numerous. Various nerve sections, differently stained, were normal. Muscles from the sole of the foot, back of the trunk, and the left calf had a hyaloid appearance, and those from the sole of the foot were striking because of the large amount of fatty connective tissue, and on account of the considerable increase in the nuclei of this tissue. The muscle fibers were small, those from the sole and the calf much smaller than those from the back of the trunk (the child had more power in the muscles of its back than in those of its lower limbs). The transverse striations were well preserved, the longitudinal not so distinct. Nerve fibers within the muscle from the sole of the foot appeared normal. The mesenteric lymph glands were much enlarged; the organs of the body were macroscopically normal.

This report strengthens the surmise of an inhibited development of the muscle fibers. Quite different, however, are the findings of Bing,<sup>10</sup> who examined a piece of excised muscle from a living child suffering from typical congenital myatonia. Examination

<sup>9</sup> This was the "ordinary concomitant convergent squint, and not an internal strabismus due to paralysis of the external rectus." (G. E. de Schweinitz, cited by Spiller.)

<sup>10</sup> Ueber atonische Zustände der kindlichen Muskulatur, *Med. Klinik*, 1907, No. 1.

of this muscle tissue showed, apart from probable increase in the nuclei, an absolutely faultless structure.

A report of the microscopic examination of the internal organs in Spiller's case was published by A. J. Smith.<sup>11</sup> The heart, pancreas, kidneys, liver, and bladder were normal. The thymus showed distinct intralobular sclerotic changes (fibrosis), with enlarged Hassal's corpuscles, and arteriosclerosis (thickening of the adventitia, occasional fibrosis of the intima, and proliferation of the endothelial cells). The spleen also showed sclerotic changes in various bloodvessels and endothelial proliferation of the Malpighian bodies. The mesenteric glands showed proliferation of the lymphatic cells.

A little patient whom I had occasion to examine with Stabsarzt Helmer, on the pediatric division of the Königlische Charité in Berlin, last year, also had this affliction. The diagnosis had been made by Dr. Reyher, who had sent the child in from the polyclinic, and who later, the child dying of pneumonia, examined some of the muscles microscopically.<sup>12</sup> His report to me was as follows: Side by side with patches of normal muscle fibers were extremely altered ones. The abnormality consisted in the cross-striation being indistinct or entirely absent. In some parts the longitudinal striation appeared to be lost. The individual muscle fibers varied very much in breadth, some being abnormally thin, others apparently abnormally broad. Where the changes were most pronounced there were but few muscle fibers to be found at all, fat and connective tissue rich in nuclei being seen instead. The changes were most marked where the clinical symptoms had been most manifest, as in the lower extremities. The long bones of the lower extremities showed considerable atrophy (which the Röntgen photogram had already shown *in vivo*). Then came the reports of a whole series of new cases, among which was one with necropsy.<sup>13</sup>

The patient was aged four months, of healthy parents (who also had another perfectly healthy four-year-old child). Parturition was normal. The infant never had had convulsions. From birth on, the neck, trunk, and all extremities appeared to be completely inert. The condition neither improved nor progressed. Examination showed a generalized flaccid paralytic condition, the muscles of bulbar innervation alone being exempt. At times a slight internal strabismus of the right eye was noticed. The facial muscles were normal. The infant sucked and swallowed well. Its cry seemed weaker than that of infants of like age. The muscles of the neck could not support the head. Those of the trunk lacked

<sup>11</sup> Histological Changes Encountered in the Thymus and Elsewhere in a Case of Congenital Hypotonia, Univ. Penna. Med. Bull., October, 1905.

<sup>12</sup> This case was to be published in full.

<sup>13</sup> A. Baudouin, La myotonie congénitale (maladie d'Oppenheim), Semaine médicale, May, 1907, No. 21.

all tonicity. The intercostals were also involved. Only in the fingers and toes did one notice movements, and these were very feeble. The feet showed varus, with slight equinus. All reflexes except those of the eye were absent. The skin, especially of the lower extremities, was wax-like and glossy, and showed a swelling resembling myxœdema. No other atrophic disturbances were present. Sensation, the sphincters, and the special senses were normal. There were no reactions of degeneration anywhere. The bony system showed neither signs of rickets nor syphilis. The child died of a bronchopneumonia, having had convulsions one hour before death. The autopsy was made twenty-four hours post mortem. The external aspect presented nothing of special interest. The muscles were pale and sunk in fat. There was considerable subcutaneous fat, in places 1 cm. thick. Microscopic examination of the nervous system showed much of interest. Sections from the convolutions of Rolando stained with the Nissl method were found normal. The nucleus of the third nerve (of both sides) was normal. That of the sixth and twelfth nerves was formed of cells well developed, many of which showed chromatolysis. Stained with the Pal and Marchi methods, the cord showed nothing abnormal. A section from the lower region of the eighth cervical segment stained with the Nissl method showed the cells of the anterior horns to be diminished in size and less numerous than normal. Those of the column of Clarke were well developed. The vessels were normal. No neuronophagia was observed. A similar condition was found in other parts of the cord. Baudouin concluded that there had been an arrest in the development of the anterior horns without any inflammatory phenomena.

A section of the anterior and posterior roots of the third lumbar segment showed a considerable difference between the thickness of the two. Normally the anterior is about one-half the size of the posterior. Here it was one-quarter to one-fifth the size. The posterior also stained much darker, the bundles of fibers having less amorphous tissue between them.

The sciatic, as an example of a peripheral nerve, showed no abnormalities by the Marchi method (no regressive or degenerative lesion therefor). The Weigert and hematein-eosin stain made manifest, however, that there were axone cylinders in the nerve not yet myelinated. There was also a slight sclerosis, and the nuclei of the sheath of Schwann were slightly more numerous than usual. The same condition was found in the crural, median, and cubital. Stained with osmic acid the right internal motor oculi is normal; the external, however, shows an absence of many myelin sheaths (the infant displayed occasional internal strabismus of the right eye). Here, too, Baudouin concludes there is an arrest in development and no neuritis. Finally, the muscle showed great changes. With weak magnification the predominating picture

was that of intense sclerosis. The stands of fibrous connective tissue within the muscle were numerous and thick. The vessels were also a little thickened, but especially interesting was the fact that they were surrounded by a zone of young cells which stained deeply, among which one noticed a rather large number of eosinophile myelocytes. As in the Charité case, one saw here bundles of very attenuated muscle fibers (measuring 6 to 8 microns) alongside of very thick hypertrophied ones (measuring 100 microns in diameter). The nuclei of the sarcoplasma were increased in number, and sometimes invaded the fiber itself. Longitudinal sections showed a disappearance of the transverse striation, the longitudinal being clear. The same picture was seen in the various muscles examined, the diaphragm, however, being the least affected. These lesions were, in Baudouin's opinion, of a regressive nature, such as one sees in the myopathies. Hystologically the skin was normal save that the subcutaneous fat was very abundant. The kidney, suprarenals, liver, and pancreas were normal. In the spleen there was a mild sclerosis. Some of the Malpighian follicles were a little more evident than normal. The thyroid presented intense sclerosis involving the acini, these being filled with cells and containing no colloid substance. No lymphatics could be seen. The thymus showed a similar sclerosis.

Finally, the gross and microscopic findings in the case of W. J. (Case III of my series) were reported by M. Rothmann<sup>14</sup> (in whose clinic the infant came to autopsy<sup>15</sup>). There was an absence of rigor mortis; the muscles all looked pale and thin. The subcutaneous fat was strongly developed. All segments of the cord showed extensive disappearance of the anterior ganglion cells, with increase in the capillaries, and atrophy of the anterior roots. In the hypoglossus nuclei there was beginning disappearance of the ganglion cells, with chromatolysis. The muscles showed atrophy and small-celled infiltration. Another case with necropsy was announced by MM. Variot and Devillers<sup>16</sup> at the Société de pédiatrie, October 15, 1907. Only a partial autopsy, it seems, was made; the results of the histological examination are still to be published.

Besides the case here communicated for the first time, some 34 or 35<sup>17</sup> cases have thus far been reported (Oppenheim 5, Berti 2,

<sup>14</sup> Dr. Rothmann had the kindness to write me, at the time the autopsy was made, that the macroscopic examination proved to be negative.

<sup>15</sup> Berl. med. Woch., November 12, 1908; Jahresver. d. Gesell. Deut. Nervenärzte, Heidel., 1908.

<sup>16</sup> Société de pédiatrie, October 15, 1907 (Archives de médecine des enfants, November, 1907, No. 11, p. 700).

<sup>17</sup> A case of Beever's (<sup>32</sup>) is cited by Collier and Wilson under their bibliography. I have not, however, been able to locate it. The case of Schüller (<sup>37</sup>) was but poorly reported, and the diagnosis, therefore, indefinite. The same may be said of a case reported by Hutinel (<sup>63</sup>).



Muggia,<sup>18</sup> Spiller, Kund,<sup>19</sup> Rosenberg,<sup>20</sup> Jovane,<sup>21</sup> each 1, Sorgente,<sup>22</sup> Comby,<sup>23</sup> each 2, Tobler,<sup>24</sup> Bing, Leclerc,<sup>25</sup> Baudouin,<sup>26</sup> Misserey,<sup>27</sup> Cattaneo,<sup>28</sup> Variot,<sup>29</sup> Reyher and Helmholz,<sup>30</sup> each 1, Haberman 2, Lugenbühl,<sup>31</sup> Beever,<sup>32</sup> Thomson,<sup>33</sup> each 1, Batten<sup>34</sup> 3, Collier and Wilson<sup>35</sup> 4). Three cases (2 by Bernhardt<sup>36</sup> and 1 by Schüller<sup>37</sup>) have been published under this heading, but do not in all probability belong here, while 1 (Carey Coombs<sup>38</sup>), though classed among the myatonic cases by Collier and Wilson, appears to me to be far too atypical to be accounted such. Another case (Wimmer<sup>39</sup>) resembles congenital hypotonic pseudoparalysis only in part, and is to be classed rather with the progressive spinal atrophies.

Studying the reports of these cases (and excepting for the time being those published in England—of which I shall presently speak) one may conclude the following: Neither sex predominates. Heredity was nil. Pregnancy and parturition were normal. In several cases foetal movements were not felt, in others they were felt precisely as in former pregnancies. In most cases nutrition was very good. In many adiposis was noticed. These children were somewhat pale and flabby, growth was normal (in no case were symptoms of rickets noticed<sup>40</sup>). The muscles were soft and doughy, but were never reported as having been truly atrophic. In one case the lower extremities felt cool and looked mottled;

<sup>18</sup> Un caso di paralisi completa congenita dei quattro arti (1° riunione dei pediatrie Piemontesi, 12 Feb., 1903, in *Pediatria*, Mars, 1903, 179).

<sup>19</sup> Ueber Myatonia congenita (Oppenheim), Diss., Leipzig, 1905.

<sup>20</sup> Ueber Myatonia congenita (Oppenheim), *Deutsch. Zeit. f. Nervenheilk.*, Band 31, 1906.

<sup>21</sup> Contributo clinico allo studio dell' atonia muscolare congenita di Oppenheim, *La Pediatria*, Mars, 1906, xiv, No. 3.

<sup>22</sup> Due casi di atonia muscolare congenita di Oppenheim, *La Pediatria*, 1906, No. 5, xiv.

<sup>23</sup> Ueber musculaire congenitale in *Archiv. de Méd. des Enfants*, 1906, Band ix, No. 9, 552; *Société de Pédiatrie*, October 15, 1907 (*Archives de médecine des enfants*, November, 1907, No. 11, 700).

<sup>24</sup> Ueber Kongenitale Muskelatonie *Jahrbuch f. Kinderheilkunde*, 1907, Band 66, Heft 1.  
<sup>25</sup> Un nouveau cas d'atonie musculaire congénitale (Maladie d'Oppenheim), *Gazette des Hôpitaux*, December 10, 1907, No. 141.

<sup>26</sup> Loc. cit.

<sup>27</sup> Myatonie Congénitale ou Maladie d'Oppenheim, Thèse, Lyon, 1908. (Same case as Leclerc, No. 25.)

<sup>28</sup> Sulle paralisi dei neonati e sulla myatonia generalizzata di Oppenheim (*Clinica moderna*, June 13, 1906, 282).

<sup>29</sup> Loc cit.

<sup>30</sup> Provisional report at the Breslau Congress for Pediatrics, 1908.

<sup>31</sup> Ein Fall von Myatonia congenita, *Deut. med. Woch.*, August 29, 1907, 1439.

<sup>32</sup> A Case of Amyotonia Congenita, *Brain*, 1907.

<sup>33</sup> A Case of Amyotonia Congenita, *Brain*, May, 1908, 160.

<sup>34</sup> Three Cases of Myopathy, Infantile Type, *Brain*, 1903, 147.

<sup>35</sup> Amyotonia Congenita, *Brain*, May, 1908, xxx.

<sup>36</sup> Zur Kenntniss der sogenannten angeborenen muskelschlaffheit, *Neurol. Centralblatt*, 1907, Heft 1.

<sup>37</sup> *Wien. klin. Wochenschr.*, June, 1904, No. 25, 722 (Verien f. Psych. u. Neurol. in Wien, May 10, 1904).

<sup>38</sup> Congenital Hypotonia (Congenital Amyoplasia), *Brit. Med. Jour.*, June 15, 1907, 1414.

<sup>39</sup> *Archiv f. Psych und Nerv.*, No. 42, 1907.

<sup>40</sup> Rosenberg's case "should have had a light attack of rickets in the eleventh month," no symptoms, however, being present at the time of examination.

in four a myxœdematous condition of the skin was described. Otherwise no trophic disturbances were noticed. The cranial nerves were always normal (in Spiller's case congenital amaurosis obtained, probably of central origin, the optic nerve being found normal). Sphincters, sensory system, and intelligence were normal. In all the patellar reflex was absent, in some the skin reflexes also. The electrical response was very much diminished or entirely absent, but never qualitatively altered. In all cases the chief symptom was the immobility of the limbs—the inactivity of the child. It appears most probable that in all cases the condition dated from birth (the only doubtful cases being Case III, which I report, and which Professor Oppenheim also thought more probably congenital, and Rosenberg's, in which the atony was first noticed in the eleventh month—the mother, however, having scarcely felt any foetal movements at all), and was in most cases noticed within the first few days after birth. In several it was only discovered later, when the first attempts at walking were made. In most cases it was found (in others the fact is not reported) that movements or "remnants" of movements were present even in the atonic muscles, if not active, then at least on pain-irritation. In a few, absolute immobility seemed to obtain (in Muggia's case in all four extremities, in Jovane's and Sorgente's cases only in the lower), and here no improvement occurred. In other cases in which at first no movement was seen this later became manifest.<sup>41</sup> One even noticed that the patellar reflex, and also single active movements set in temporarily after energetic faradization.

Many cases (12) showed improvement after long-continued treatment (Rosenberg reports improvement even after thirty-one months). In others no improvement occurred. In several cases the outcome is not known. In our third case an exacerbation was noticed in the fifth to sixth month. In no other case was the condition noticed to progress. In 11, death occurred immediately, due to pulmonary disease (pneumonia). Three cases had convulsions. This occurred in Sorgente's 2 cases (both of the same parents), in the one, tonic and clonic spasms of all the limbs five hours before death; in the other, generalized convulsions twice in the last twenty-four hours; in Baudouin's case, one hour before death. Sorgente's cases suggest that the condition may occur familialy.

In all the cases the lower extremities were affected; in more than half the upper also (though usually in lesser degree); in many the trunk besides; in five, also the head; in two, the diaphragm seemed affected; in three, strabismus was present; in one, the

<sup>41</sup> It may here be remarked that in some of the histories little attention was paid to these slight movements in the muscle groups, or the fact was not reported. In all cases which were carefully examined and minutely reported the fact is emphasized that nowhere did absolute immobility obtain, so that we may conclude that actual paralysis occurred in no case, only varying degrees of atony.

facial muscle appeared somewhat weak. Throat and cranial nerves, therefore, appear on the whole to be free. Never when movements were executed was coördination disturbed. Standing and walking were in no case possible. Most all showed a functional kyphosis usually very intense in sitting. In two, atrophy of the bones of the lower limbs was noticed. Once, secondary contraction (in the hand). The distal parts were always less affected than the proximal, and were even entirely free in several cases of severe proximal involvement. Slight cases showed hypotonicity only; severe cases absolute atony. In most cases the teeth showed no abnormality; in one or two, teething was late. Subjective symptoms do not appear to occur.

The majority of the cases reported in England (Batten, Collier and Wilson, Coombs, Thomson) are of older children (five to ten years of age). In most of these contractures were noticed (doubtlessly due to the long continuance of the disease). The affected muscles are defined as being small and thin, and the description suggests considerable wasting, even though no real atrophy should have occurred. In no case was adiposis present (this period of childhood being less prone to adiposis than the first two years). These authors emphasize the long, narrow, pad-like formation of the feet and hands. The joints are especially hyperextensive. Certain of these cases show discrepancies which make them somewhat doubtful. Thomson's evidently had a difficult partus (under chloroform). The mother complained of the child being drowsy. The hamstrings and adductors of the thigh did not appear to be affected (distribution?). There was little difference between CCC and ACC. Finally, the patellar reflexes were present, and the improvement was so rapid that the child could sit up and make attempts to walk after four months. One case of Collier and Wilson's was well up to the twelfth month. These authors speak of a prenatal type, and even assume the occurrence of this disease after acute illness in a previously healthy child. The major evidence as yet in hand is, I believe, against this inference. Coombs' case is certainly too atypical to belong here. The child was ten years old. The condition was first noticed in one hand, and only months after in the rest of the body. The distal muscles suffered more than the proximal. The scapulæ were winged. The knee-jerks were present and brisk. The Achilles phenomenon was also present.

The clinical picture of myatonia congenita is, on the whole, therefore, a typical one, and may roughly be landmarked as a congenital, atonic pseudoparalysis, met with in children in the first two or three years of childhood, in which the reflexes are very weak or abolished, electrical reaction reduced but never degenerative. real atrophy not met with, the distribution proximal, with no progression, the muscles of bulbar innervation practically exempt,

and no sensory, bladder, nor rectal involvement occurring. In a minimal group the children are older, contractures are present, the muscles small and thin (atrophic?).

Coming to the differential diagnosis of this disease, we must first consider those conditions in which we often meet with a high degree of muscular atony—namely, infantile or congenital myxœdema, mongolianism, and, above all, rickets. Among our cases we have, in fact, four (cases of Baudouin, Leclerc, Berti) which showed myxœdematous thickening of the skin: while in one (Baudouin's) the autopsy displayed gross changes in the thyroid gland. And yet I believe we may exclude myxœdema entirely. In the first place, this symptom complex is typical: the characteristic physiognomy; the small, widely separated eyes; the spare hair growth; the swelling about the face, forehead, and especially the eyes (regions not at all affected in three of the cases above referred to); the pallor or wax-yellow sallowness of the skin, and it's great dryness (often scaling); the thick tongue, usually protruding from the mouth; the umbilical hernia, obtaining in all cases of any severity; the persistent patency of the large fontanelle; the impaired psychic condition; the pronounced disproportion between length and breadth of the body; and finally, the fact that myxœdema is unusual in boys, and that only one of the myatonia cases observed (Baudouin's) bears the slightest resemblance to it. On the other hand, no condition described as arising actually or experimentally from thyroid insufficiency<sup>42</sup> has any likeness to Oppenheim's disease.

As regards mongoloid idiocy, it may be dismissed without comment, as it gives so typical a picture that it could scarcely be mistaken for anything else.

Rachitis, however, we must study more carefully, as this disease often evidences a high degree of hypotonicity, which may easily enough be taken for paralysis. Rickety limbs may occasionally be placed in all sorts of abnormal and uncomfortable positions without causing distress to the young patients. They may in some cases even be twisted about after the fashion of the circus "snake-man," strongly hyperextended and shown to be loose and wobbly like flails. This pseudoparalytic condition occurring in rickets has been described by Oppenheim,<sup>43</sup> Comby,<sup>44</sup> Vierordt,<sup>45</sup> Hagenbach-Burckhardt,<sup>46</sup> and Bing.<sup>47</sup> One may also find a slight muscular

<sup>42</sup> Ewald in Nothnagel's System, Band xxii; Kassowitz, Infantile Myxœdem, etc. Vienna, 1902; Magnus-Levy, *Organotherapie und Innere Secretion*, 1906; Krehl, *Ueber die Störung chemischer Korrelationen im Organismus*, 1907; Anton, *Entwicklungsstörungen beim Kinde*, Berlin, 1908.

<sup>43</sup> Lehrbuch, second edition.

<sup>44</sup> Grancher's *Traité des maladies de l'enfance*, tome iv.

<sup>45</sup> *Ueber Hemmungslähmungen im frühen Kindesalter*, Deutsch. Zeit. f. Nervenhe., 1900, Band xviii, S. 167.

<sup>46</sup> *Klinische Beobachtungen über die Muskulatur der Rachitischen*, Jahrb. f. Kinderheil., 1904, lx, Heft 3.

<sup>47</sup> Loc. cit.

atrophy in these cases not easily noticed because of the frequent adiposis present. Whether such fully developed condition of rickets can be present at birth is highly questionable, and has up to recently been the cause of much controversy. Escher,<sup>48</sup> who undertook the microscopic examination of sections from a large number of apparently rachitic newborn infants, could at no time find any changes which would substantiate the diagnosis of rickets. Heubner<sup>49</sup> holds that one will rarely if ever be able to make the diagnosis of congenital rickets if one believes with Pommer (with whom he likewise agrees) that a retarded bone development, a standing still in the half-completed stage, is the cardinal feature in rickets. And Stoeltzner<sup>50</sup> says that no unchallengeable case of congenital rickets has yet been recorded. Most conclusive, however, has been that painstaking study of nearly a thousand newborn infants by E. Wieland,<sup>51</sup> of Basel, undertaken, as he tells us, to prove the positive side of this question, but which led to an absolute negation. He shows how former mistakes were made in judging the costocartilage nodes (*Kantenbildung*) so often met with in the newborn, to be rachitic ("rosary"). These are normal occurrences, especially pronounced in strong muscular babies (so also Feyerabend, Cohn, Spietschka, Escher, and Tschistowitsch). Another symptom which led astray was the so-called "cranio-tabes." This symptom he found present in 18 per cent. of his material (that is, in 182 of the 1000 cases), a number of these also showing bone defects, the infants being otherwise absolutely normal and not developing any signs of rickets (these cases being followed up from one to two years). He believes that the condition of "soft skull" is a "pathology" *sui generis*, occurring in weak children, and having no connection with rickets. Wieland's analysis leads us to conclude that rickets cannot be clinically demonstrated in the newborn, and that in all probability not the disease itself but only the disposition to it may be congenital. We may therefore say that in the majority of cases of myatonia congenita the condition is noticed within the first few days or weeks post partum, this never occurring in rickets. In most of the cases of rachitic pseudo-paralysis observed by Vierordt<sup>52</sup> the children had already learned to stand or walk, only again to "unlearn" it. The rachitic child does not make attempts at walking, but, contrary to the normal infant, draws up its legs and usually shows resentment (irritability) to passive motion. In myatonia no rickety symptoms have thus far been reported. And finally, this fact of interest may be noted,

<sup>48</sup> Escher, *Zur Frage der angeborenen Rachitis*, *Jahrbuch f. Kinderheil.*, Band lvi, S. 613.

<sup>49</sup> *Lehrbuch*, Band i, S. 667, 668.

<sup>50</sup> *Handbuch d. Kinderheil.* of Pfaundler u. Schlossmann, Band i, 605.

<sup>51</sup> *Klinische Untersuchungen über Frührachitis*, *Deut. med. Woch.*, September 3, No. 36, 1545.

<sup>52</sup> *Loc. cit.*

that the study of rickets undertaken in Hagenback's clinic at Basel showed that the tendon reflexes in this disease are never absent, but even exaggerated at times, while in myatonia congenita they are always absent.<sup>53</sup>

But little need be said concerning the "inhibition paralyses" ("Hemmungslähmungen") of Vierordt.<sup>54</sup> These are pseudo-paralyses due to pain, occurring in Barlow's disease, in hereditary syphilis (Parrot's disease), and also in rickets, as already described. As they are due to pain, the very examination will call forth muscular spasm (Oppenheim). Besides, it has been pointed out that syphilitic pseudoparalysis very rarely affects the lower extremities.<sup>55</sup> The history of these cases would also show that the paralysis did not date from birth (only one congenital case has been reported<sup>56</sup>), and that symptoms of syphilis are present, or were so a few weeks previously.<sup>57</sup> Infantile scurvy would also give its symptoms (swollen gums, tendency to hemorrhage, etc.), and the history would probably point to error in diet. Only once, to my mind, has a painless pseudoparalysis due to scurvy been mentioned.<sup>58</sup> The disease is never congenital. In myatonia congenita no symptoms of scurvy or syphilis have been noticed, no pain seems to have been present, and the affliction has been preëminently in the lower extremities.

As to polyneuritis, only that due to diphtheria could come into question, and in fact only the nasal type, in which the diphtheria might be overlooked and the history give no account of it. Then, too, diphtheritic polyneuritis within the first two years of infancy is a rarity. The muscles here affected would give the reaction of degeneration.

Paralysis due to poliomyelitis, even if not congenital, has been seen to occur early (one case of Duchenne on the twelfth day, one of Zappert on the fifteenth, one of Sinkler in the sixth week), though such early cases are extremely rare. It is easily differentiated from myatonia by the atrophy and trophic disturbance, the reaction of degeneration, the course of the disease, and in the fact that poliomyelitic paralysis occurs after an acute illness in a previously healthy child. This disease is rarely symmetrical, myatonia congenita probably always; and finally, infantile spinal paralysis improves rapidly, only a (small) part of the original paralytic

<sup>53</sup> The knee-jerk was reported present in Thomson's case, though nothing is said of its character. This case is not entirely unchallengeable.

<sup>54</sup> Loc. cit.

<sup>55</sup> Hutchinson, *Lectures on Diseases of Children*, London, 1906.

<sup>56</sup> Vicarelli, *Revue Mens.*, Mars, 1892.

<sup>57</sup> This was noticed in a case of Oberwarth (*Zur Kenntnis der syphilitischen pseudoparalysis*, *Jahrbuch f. Kinderh.*, 1899, Band xlix). It is also interesting to note that in a few cases of this series no swelling could be felt in the involved limbs, and in four cases there was no pain on pressure or passive motion.

<sup>58</sup> Vierordt, loc. cit.

involvement remaining permanent—the improvement in *myatonia* being very slow, and general, not in any single limb.

We may exclude the possibility of a spinal hemorrhage (*hematomyelia*) entirely, as there are no sensory disturbances, nor affection of the bladder and rectum, nor decubitus. Nor is there anything in the etiology to suggest it (forceps, difficult labor, convulsions, scurvy, infectious disease). Should, however, the possibility of spontaneous hemorrhage in utero be admitted (such hemorrhages occur in the adult), and we surmise that such hemorrhage has occurred in the anterior horns alone, antepartum, we would expect to find a degenerative paralysis present—in other words, the picture of congenital anterior poliomyelitis—which, as we have already concluded, does not appear ever to have been seen.

We finally come to the consideration of two conditions which have been associated by one or two writers on this subject with our congenital hypotonic pseudoparalysis, and which, in view of Baudouin's pathological findings, are especially interesting in this connection. The first is a motornuclei aplasia, and the second is the spinal type of muscular atrophy, with which we may also consider the muscular dystrophies.

There is a pathological condition which manifests itself through paresis or paralysis of the muscles of the eyeball (*ophthalmoplegia*), through atrophy of the tongue, through inadequacy of facial mimic, etc. Sometimes all these symptoms are present, sometimes only one or two, as *ophthalmoplegia* or ptosis alone. These symptoms correspond to a lesion in the nuclei of the oculomotor, facial, hypoglossal, etc., and were thought by Möbius<sup>59</sup> to be due to an absence or partial development of the bulbar motor nuclei ("Infantiler Kernschwund"). Heubner,<sup>60</sup> in an autopsied case, was able to prove the correctness of this surmise (though it appears that some of these cases may be due to a congenital lesion anywhere along the tract between the motor nuclei and the muscle<sup>61</sup>). That a similar aplasia or hypoplasia of the anterior horn cells in the lumbar or cervical segments might occur does not seem impossible, but no such case substantiated by autopsy or case even suggesting such occurrence have I been able to find in the literature,<sup>62</sup> and the autopsies of Spiller showed no trace of spinal involvement, while that of Baudouin showed that much else apart from the anterior horn cells was pathologically affected. Muggia thought that some type of spinal

<sup>59</sup> Münch. med. Woch., 1892.

<sup>60</sup> Berlin. klin. Woch., 1890. See also Lehrbuch, ii, 124, 125.

<sup>61</sup> Kunz, Beit. z. Augenheilkunde, Nos. 35 and 37 (cited by Zappert). See also Oppenheim, Lehrbuch, p. 1033.

<sup>62</sup> Heubner (Lehrbuch, ii, 124) speaks of being able at times to find a muscle wanting in other parts of the body having nothing to do with the bulbar nuclei (as the pectoralis major). The pectoralis as an isolated congenital defect, however, appears not to be uncommon. The literature has over a hundred cases. The combination with other muscle defects is rare. See especially Ziehen, Beziehungen zwischen angeborenen Muskeldefekten, infantilen Kernschwund, etc., Berl. klin. Woch., No. 34, August 24, 1908.

aplasia might be the underlying cause in his case, though this was only a clinical observation. Just what he meant is not certain, though Rosenberg points out, that should he have implied an inhibition to ganglion cell growth ("Entwicklungshemmung") then this idea would be in keeping with Oppenheim's theory.

Of the dystrophies, we may say that the various types are usually (though not always) hereditary or familial—myatonia congenita being in but one instance familial<sup>63</sup> (Sorgente's two cases)—they are never congenital, they usually evidence severe atrophy, and generally affect the pelvic and lumbar musculature first, while the infantile type is earliest noticed in the face. Such distribution is not found in Oppenheim's disease. Electrically both conditions are not to be distinguished from each other, and in both a pseudohypotrophic form may occur because of adiposis, yet never has myatonia congenita resembled the typical picture of muscular dystrophy. Never has a case of muscular dystrophy improved as several myatonia cases have, nor have the patellar reflexes been seen to return in the former, as occasionally reported in the latter. Finally, and this is of greatest importance, the dystrophies are eminently progressive.

Much the same may be said of "early infantile spinal progressive muscle atrophy" (Werdnig and Hoffmann). This very uncommon disease (only about thirty cases have thus far been described) is exquisitely familial and hereditary (in one family six of fifteen children, in another three of six were affected; in one family in which three children were affected, eight brothers and sisters of the mother had died of the same disease). In this one fact it differs markedly from myatonia congenita, in all of which cases, with one exception (Sorgente's two cases in one family), there was no trace of any hereditary or familial tendency. Furthermore, as the majority of our myatonia cases are absolutely congenital; the cases of Werdnig, Hoffmann, and Bruns were all prenatal, beginning usually in the second half of the first year, in a few in the second year. Again all these cases were progressive and fatal, death occurring within two to four or five years. This progression showed itself in a spreading of the paralysis (beginning in the muscles of the pelvic girdle and thighs, gradually involving those of the trunk, shoulder girdle, neck, and, finally, the hands and feet). Parallel with the paralysis goes the atrophy, which becomes excessive. In no case of Oppenheim's disease has such progression been noticed, nor an outspoken atrophy. Nor was reaction of degeneration reported, though this was partially or completely present in a number of the Werdnig and Hoffmann type of cases. From this account it will be seen that though both diseases show

<sup>63</sup> Because of this very fact, Collier and Wilson do not wish to count Sorgente's cases to those of myatonia congenita.



a flaccid condition, with loss of tendon reflexes, a sparing of sensory, bladder, and rectal involvement, as well as of the muscular area innervated by cranial nerves, there is decided enough difference between them to diagnosticate separate clinical entities. The question, however, arises, Are there transition stages (Uebergangsformen) between the two conditions? Wimmer thought that his case was such,<sup>64</sup> and assumed that this disease constituted a condition in which a congenital resistentia minor obtained, which in several cases was temporary and reparable (Oppenheim's myatonia), in others progressive and lethal (Werdnig and Hoffmann's muscle-atrophy). And Rothmann<sup>65</sup> also maintained that the majority of myatonia cases are due to a lesion in the ganglion cells of the anterior horns occurring in foetal life, which may vary in severity up to complete aplasia, and that between the myatonia of Oppenheim and the muscle atrophy of Hoffmann, all grades of transition cases occur, which are not to be sharply differentiated, though one may place the abating and improving myatonia cases apart from the increasing and pernicious spinal atrophies; and finally, that it is evident that transitions occur between the congenital spinal muscle atrophy with involvement of the bulbar nuclei and Möbius' infantile nuclei aplasia. Now, these seem to be interesting assumptions, though there appears to be too little in the data up to now available to substantiate them. The severe cases of myatonia did not gradually become so; the condition was seen in full development at or very soon after birth. Even in these severe cases no reaction of degeneration was present, nor was special atrophy seen; and Spiller's autopsy revealed nothing pathological in the nervous system of a pronouncedly affected case. This argues strongly against the spinal origin of the disease. On the other hand, the pathological findings reported by Baudouin speak for an arrest in the development, while the findings in the Werdnig and Hoffmann cases showed an outspoken atrophic degeneration of the entire spinomuscular neurone and terminating muscle.<sup>66</sup>

Interesting, too, is Bing's surmise that behind the myatonic condition may lie an inhibition not of muscle development, but of the tracts responsible for the regulation of muscle tonus—namely, the spinocerebellar tract. These tracts, however, were found in Baudouin's case to be intact. Berti, Cattaneo, and Baudouin thought that a congenital alteration in the internal secretion, probably hypofunction of the thyroid, was the cause of this disease. The thyroid gland in Baudouin's case did show extreme sclerosis. Is this, however, a chance concomitant occur-

<sup>64</sup> The case was congenital, the atrophy and weakness progressive. The electrical reaction was much reduced, the galvanic tardy and with very little difference between CCC and ACC.

<sup>65</sup> Loc cit.

<sup>66</sup> Leyden-Goldscheider, *Erkrankungen des Rückenmarkes*, Nothnagel, Wien, 1904.

rence, is it cause, or is it effect? There is no way of telling, though there is too much, as we have already seen, against the theory of thyroid hyposecretion to consider it as cause of the condition. And I may add to what I have already said under the differential diagnosis of myxoedema—and this applies to internal hyposecretion of thymus and adrenals—that one would expect in such disturbance an affection of the entire muscular system, and not of any special group of muscles (with sparing of other groups, as the distal muscles, those of bulbar innervation, etc.), as is the case in myatonia congenita.

Upon the thought of a thymic syndrome (Smith), we can scarcely comment, as we know little or nothing about the thymus. It appears that a fibrosis of this gland is commonly associated with idiopathic infantile atrophies (Fortescue-Brickdale, Dudgeon<sup>67</sup>).

Very little can also be said of the microscopic muscle findings. These are not typical, but similar in large measure to those in the dystrophies and spinal atrophies. Furthermore, we know too little about foetal and early infantile muscle conditions (there is really no literature to be found upon the subject) to determine to what extent these findings are to be considered pathological.

At the finale, therefore, we are left with our pathological problem unsolved. The few autopsy examinations which have been made lead us to believe the muscle changes to be secondary, not, however, to degenerative changes in the ganglion cells of the anterior horn, but to a retarded development of these or to a congenitally enfeebled or enervated condition—capable of developing, of improving, of regaining their “trophic virility.” Whether in some cases these spinal cells are congenitally abiotrophic (the word is Gowers’), destined to degenerate and atrophy, it is as yet impossible to say. Of one thing we are, however, certain, and that is that this myatonia congenita of Oppenheim’s is a new clinical entity, in its typical form a sharply defined syndrome differentiable from all the heretofore-known myopathies and spinal atrophies, constituting a congenital atonic or hypotonic, pseudoparalytic condition seen mostly in children within the first two years of infancy, associated with loss of tendon reflexes, without reaction of degeneration and atrophy, of proximal distribution, always affecting the lower yet often the upper extremities, trunk and neck beside, but not the muscles of bulbar innervation, and showing a tendency to spontaneous though slow improvement (hastened in many cases under massage and electrical treatment).

<sup>67</sup> Cited by Carey Coombs.

<sup>68</sup> Bull. de la Société de pédiatrie de Paris, Février-Mars, 1899.

<sup>69</sup> Lévi-Singue, L’atonie Musculaire Congénitale, Gazette des Hôpitaux, No. 15, Février, 1909.

## SYPHILITIC PARALYSIS OF THE TRIGEMINAL NERVE.

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THE trigeminal nerve is seldom paralyzed without implication of other cranial nerves, and the suspicion is occasionally entertained that syphilis may be the cause of this paralysis. It is important to know the frequency of syphilitic disease of this nerve, especially of paralysis confined to this nerve. We have several times found bilateral degeneration of the trigeminal nerve, including the spinal root, in tabes.

Oppenheim<sup>1</sup> refers to a long list of authors who speak of implication of the trigeminal nerve in cerebral syphilis, but apparently he is referring chiefly to the clinical manifestations, although he mentions that he has had confirmatory pathological findings. In one of his cases the spinal root of this nerve was affected, as it was also in a case reported by Brasch, and in one reported by F. Pick. According to Uhthoff's statistics, the trigeminal nerve seems to be implicated in syphilis as often as the abducent nerve, that is, in 14 per cent. of all cases of cerebral syphilis. Usually the implication of this nerve is unilateral, although exceptions to this rule occur (Leudet and Labarrière, Hutchinson). The sensory branch is much more frequently affected than the motor. Pronounced paralysis of the muscles of mastication with atrophy has occurred very exceptionally (v. Ziemssen, Loewenfeld, Oppenheim).

Nonne<sup>2</sup> states that Huguenin found gumma of the Gasserian ganglion; Balfour, gumma of the sella turcica, with pressure on the trigeminal nerve; and Uhthoff, in 37 necropsies in which the trigeminal nerve was found diseased, observed involvement of this nerve alone only in four. Degeneration of the spinal root of the trigeminal nerve in cerebral syphilis he states has been observed by Oppenheim, F. Pick, Brasch, and Cassirer. In all these cases the involvement of the nerve was unilateral. In Pick's case the trigeminal nerve was implicated in a gumma, in Cassirer's the cause was

<sup>1</sup> Oppenheim. Nothnagel's System of Medicine.<sup>2</sup> Syphilis und Nervensystem, second edition, p. 233.

intense basal meningitis, in Oppenheim's and in Pick's the Gasserian ganglion was diseased.

Recently one of us (Spiller) has seen a case of cerebral syphilis in consultation with Dr. S. R. Crothers, in which left hemiparesis was associated with partial palsy of the third nerves and weakness of the motor branch of the right trigeminal nerve. The sensory branch of the trigeminal nerve was not affected. When hemiplegia from syphilis is associated with paralysis of cranial nerves, two lesions usually are found as the causes of the symptoms: a basal syphilitic meningitis producing the cranial nerve palsies, and arteritis producing occlusion of a bloodvessel with softening in the region of the internal capsule.

Five years ago a case of syphilitic disease of the fifth nerve was studied clinically by one of us (Spiller) and later the microscopic examination was conducted by us conjointly. The extraordinary fibrillary tremors of the right masseter muscle indicated that this muscle was in a condition of acute degeneration. So far as could be determined from the history and the examination, the only cranial nerve affected was the fifth on the right side, although the eye-grounds were not examined; and this fifth nerve palsy was associated with recent right hemiplegia implicating the right side of the face as well as the limbs. The palsy of the fifth nerve was inferred from the intense fibrillary contractions confined to the masseter muscle, as the man was too unconscious to respond to tests, and confirmation was obtained by the microscopic examination. No statement is made as to fibrillary contractions in the right temporal muscle, although they may have been present. The palsy affected the motor branch, and this is more uncommon than is implication of the sensory branch, but from the history it is probable that the sensory branch did not escape, as it is stated that he had pain on one side of the face. No gross lesion explanatory of the fifth nerve palsy was recorded in the notes taken by the pathologist (Dr. Alburger) who performed the necropsy, and it is probable, therefore, that it was caused by the intense syphilitic meningitis found by the microscope.

W. L., laboratory number 111, male, aged thirty-five years, colored, was admitted to the service of Dr. Stengel, March 2, 1904. About one year previously he had a stroke involving the left upper limb, which was partially paralyzed, and from this he never entirely recovered. He always dragged the left lower limb slightly after this attack.

He had suffered from "neuralgic" headaches, as he called them, a number of years. The pain was usually on one side of the face and head. It is presumable that it was on the right side, although it is not so stated. He seemed well four days before admission to the hospital. On the evening of February 29 he complained of headache, but seemed well the following day and went to work,

but had to stop work because of the headache; about six o'clock his friends noticed that he could not speak, although he was still able to walk about, and he ate moderately at the evening meal. He retired soon after dinner; on the following morning he was unable to get out of bed, and was unconscious; he could not answer questions, and could take neither water nor food.

Notes taken by Dr. Spiller shortly after his admission to the hospital are as follows: The patient is unconscious. When he is called by name he opens his eyes, but makes no sign of understanding what is said to him. He does not open his eyes very widely. The eyeballs are not deviated. He is able to look upward and to the left, but it is impossible to test the movements of the eyeballs carefully. He closes the eyelids firmly on each side, and seems to have a little flattening of the lower part of the right side of the face.

When he is told to show his teeth he attempts to do so, and the lower part of the face is moved only on the left side. He has, therefore, paralysis of the lower part of the right side of the face, but it is impossible to get him to show the tongue. The right side of the face does not contract when it is stuck with a pin, but marked contraction occurs on the left side of the face. Very intense fibrillary contractions occur continually in the right masseter muscle. The contraction of the masseter muscles cannot be tested, as it is impossible to get the man to make chewing movements.

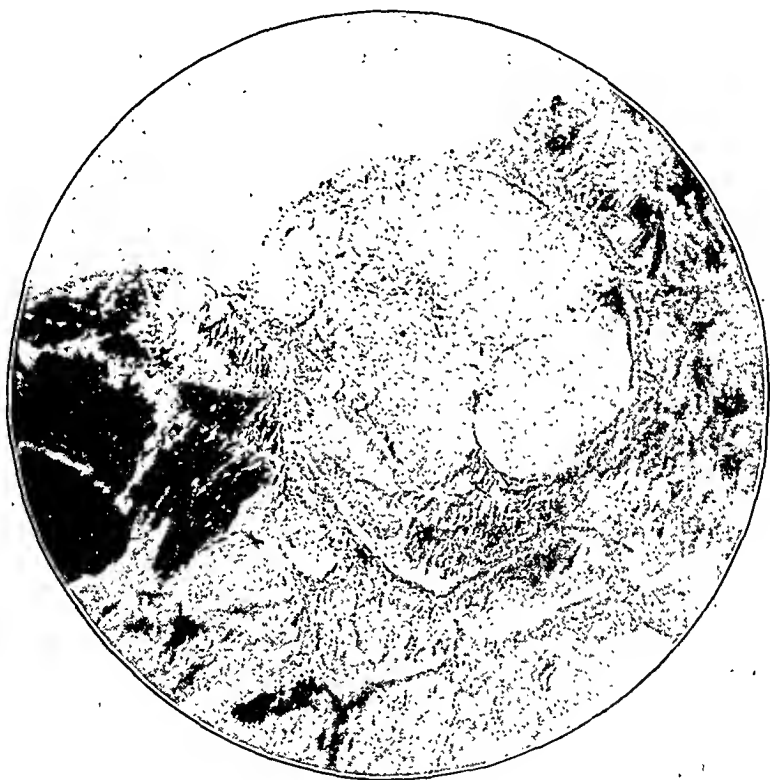
Upper limbs: He raises the left upper limb freely above the head. The right upper limb is in slightly increased tonicity. The biceps-tendon and triceps-tendon jerks and wrist reflexes are exaggerated on the right side. The corresponding reflexes on the left side are about normal. When the right upper limb is stuck with a pin very little attempt is made to move it, but he tries unsuccessfully to find the source of irritation with the left hand. Sensation for pain is probably preserved in each upper limb. The left upper limb is somewhat spastic.

Lower Limbs: The right lower limb is paralyzed. He can flex the right thigh slightly when the limb is stuck with a pin, and can flex the right knee slightly. The left lower limb is moved freely. The pinprick is perceived well in each lower limb. The right patellar reflex is exaggerated; the left is about normal. The Achilles jerk seems to be about normal on each side. A slight indication of ankle clonus is obtained on the right side. Babinski's reflex is not obtained on the right side, the toes not being moved at all. It is obtained on the left side, all the toes except the big toe being distinctly moved upward. The right lower limb is somewhat spastic, the left is about normal.

The man died shortly after admission to the hospital.

An area of softening was found in the left temporal lobe. Sections stained with the hemalum and acid fuchsin showed an intense

round-cell infiltration and numerous fatty granular cells in this region. This lesion was probably the cause of the right hemiplegia. Slight degeneration was found in the left anterior pyramid and marked degeneration in the right anterior pyramid by the Marchi stain. Probably sufficient time before death had not elapsed for intense degeneration of the left anterior pyramid, detectable by the osmic acid, to occur.



Section of the roots of the right trigeminal nerve, showing an area almost completely degenerated (Weigert stain.)

Sections of the roots of the right fifth nerve showed much degeneration when stained by the Weigert method or by acid fuchsin with hemalum, and in some parts of the sections the nerve fibers had entirely disappeared. Recent degeneration was revealed by the Marchi method in the right fifth nerve within the pons and within the spinal root of this nerve. The pia over the pons, optic chiasm, and optic nerves presented intense round-cell infiltration. The left crossed pyramidal tract was more degenerated than the right.

We are indebted to Dr. Allan J. Smith for the photograph.

## THE PATHOLOGY OF THE CRANIAL NERVES IN TABES DORSALIS.<sup>1</sup>

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SYMPTOMS referable to the oculomotor and especially to the abducens nerves are very frequent and often precocious in tabes dorsalis, and it is strange that the anatomical changes underlying these have so long escaped detection. The transitoriness of many cases of diplopia occurring in tabes has been believed to account for this, but this argument is invalid in cases in which the strabismus is permanent, and such cases are not infrequent. The cause of the Argyll-Robertson pupil has been a constant puzzle to neurologists, and it still remains so, as we are not yet sufficiently informed of the course of the fibers subserving the reaction of the pupil to light. This paper will not solve that riddle, although the facts herein presented may afford a substratum for future research concerning iridoplegia in tabes. Regarding oculomotor paralysis, at least, the facts here presented demonstrate the morbid anatomy and appear to solve the pathogenesis. Read in conjunction with preceding articles,<sup>2</sup> they very fully show the etiology, mode of genesis, and microscopic appearances of the cranial nerve palsies occurring in tabetics and paretics, both at their inception and after the disability has become permanent. The facts add one more stone to the edifice of the luetic origin of taboparesis, and afford another illustration of the explanation offered by Nageotte<sup>3</sup> as to the pathogenesis of those disorders.

**THE INITIAL LESION OF TABES.** It will be remembered that as long ago as 1894<sup>4</sup> the French neurologist presented preparations showing that the initial lesion of tabes dorsalis consist. of a chronic inflammation of the posterior and often the anterior spinal roots—a transverse radiculitis. He showed that the seat of election of this process is the situation where the anterior and posterior spinal roots, in approaching one another, are surrounded by the funnel-shaped prolongation of the meninges which cover them before being

<sup>1</sup> Through the kindness and courtesy of Dr. Clovis Vincent, of Paris, I have been enabled in this article and in a preceding one (*New York Medical Record*, January 29, 1910) to place before American readers the main data of the two sets of investigations which Dr. Vincent has been pursuing during the last five years in the clinics of the Parisian hospitals, La Pitié, La Salpêtrière, and St. Louis, and in the laboratories of Babinski and Nageotte, Raymond, and Chauffard. The reader will see that the results of Dr. Vincent's researches afford still further corroboration of the ideas so long upheld by Babinski and Nageotte, that all the symptoms of taboparesis ensue upon a chronic meningitis of syphilitic nature. The data here expounded clearly show the untenability of the dystrophie theory of taboparesis.

<sup>2</sup> *Medical Record*, January 29, 1910; *AMER. JOUR. MED. SCI.*, August, 1908.

<sup>3</sup> *La Pathogénie du Tabes Dorsalis*, Paris, 1904.

<sup>4</sup> *La Pathogénie du Tabes Dorsalis*, Paris, 1904.; *Soc. Méd. des Hôp.*, 1894.

pierced by them at their exit from the theca vertebralis. The gradual approximation of the meninges at this spot, he believed, produced a concentration of toxic or inflammatory materials around the nerve fibers traversing what he called the radicular zone. An arachnoiditis became a perineuritis, and finally spread into an endoneuritis. It was to this process that was due the degeneration of the posterior columns of the spinal cord. Although the anterior roots participated, their power of regeneration frequently prevented permanent paralysis and muscular atrophy; but perhaps 20 per cent. of tabetics did show some muscular atrophy sooner or later.

As a preliminary to what is to follow, no more than this need be said, for Nageotte's preparations are figured and the evidence presented in some detail in a previous article,<sup>5</sup> and in a shortly forthcoming communication<sup>6</sup> the further questions are taken up regarding the recent biochemical hypotheses which Mott<sup>7</sup> has advanced to reconcile the syphilitic etiology of tabes with the dystrophic theory so long held by the majority of English and German neurologists.

REFLEX IRIDOPLEGIA AND THE SYMPATHETIC NERVE. Future research as to the pathogenesis of the Argyll-Robertson pupil, that long-standing puzzle of neurologists, may find its direction in the lines of this investigation, for it will be noted in Vincent's case that there was no examination of the sympathetic fibers in and around the cavernous sinus, for, of course, the almost complete ophthalmoplegia could itself account for the iridoplegia of this patient. But if studies of this kind fail to reveal, in cases showing the Argyll-Robertson pupil, any lesions of the third nerve and lenticular nucleus, the incrimination of the sympathetic might be probable, for Roux<sup>8</sup> has shown how, in the spinal region, the sympathetic fibers are very often attacked in tabetics en route from the cord to the ganglionated chain, and that they are attacked as they traverse the radicular zone of Nageotte along with the sensory or motor fibers of the cerebrospinal system.

The mechanism of the light reflex is not yet decided. It has been considered a simple sensorimotor one, and its mechanism sought for along the arc, afferent optic fibers, synapse neurone, efferent third nerve fibers, for it is abolished by destruction of any of these. But we are by no means certain that it may not be an inhibitory phenomenon due to an arrest by the stimulus of light of the dilatatory impulses of some part of the ciliospinal or other mechanism travelling by the cranial sympathetic. In that case we should interpret the light reaction as due to a withdrawal of the antagonizing tonus of the dilator iridis from the balancing tonus of sphincter iridis, whereby the latter prevails and produces pupillary contraction; but it can do so, of course, only when its fibers in the third nerve are intact

<sup>5</sup> AMER. JOUR. MED. SCI., August, 1908; also Brit. Med. Jour., October, 1909.

<sup>6</sup> International Clinics, Spring, 1910.

<sup>8</sup> Thèse de Paris, 1900.

<sup>7</sup> Brit. Med. Jour., 1909, i.



and when an afferent stimulus is possible. But if at the state of rest the sphincter tonus is unopposed from paralysis of the dilator, of course contracture of the pupil remains constant, because unopposed, and naturally the dilator afflux, already removed by disease, will not be influenced by light. In other words, an Argyll-Robertson pupil would be one that does not dilate in the absence of light.

Some tabetics' pupils are fixed in dilatation, which, on the theory now promulgated, would be explained by interference with the third nerve afflux by meningitic processes, thus leaving the dilator tonus in full sway; though it is hard to explain why such pupils do not further dilate in the absence of light (if, indeed, they do not), and thus give the appearance of contracting to the stimulus of light. At all events, it is hardly likely that a meningeal inflammation so widespread as that which causes tabes could fail to implicate some of the sympathetic fibers in their course in the cranial cavity. The difficulties of the research should be obvious, but in these days of serial sections they should not be insurmountable. It is possible, too, that the sympathetic contains sphincter fibers also, for Jegorow<sup>9</sup> states that he found greater dilatation of the pupil after excision of the ciliary ganglion than he did after proximal cutting of the third nerve; and François-Franck,<sup>10</sup> too, found that cutting the ciliary nerves caused greater dilatation than did cutting the third nerve.

**THE CASE.** In the case now to be described,<sup>11</sup> a meningitis of long standing, no longer in activity, had left its traces merely in hyperplasia of the connective tissue of the nerve and partial destruction of the noble elements. The patient was a woman, aged fifty-one years, married at eighteen, with five healthy children and two miscarriages, the last in 1885, accompanied by sore throat and followed by an attack of headache, delirium, convulsions, and coma. It was most probably a meningitis, for she remained quite blind, and had frequent attacks of focal epilepsy on the left side.<sup>12</sup> In 1891 Gombault had found psoriasis, blindness, laryngeal trouble, and focal epilepsy, the last disappearing. On admission the nutrition was good. There was a syphilitic perforation of the palate. There was gray atrophy of the optic papillæ, with contraction of the vessels. Even light was unperceived. There was partial ptosis, especially of the left lid. Ocular convergence was impossible. Internal lateral movements could not be accomplished, nor could the raising or lowering of the globes; but the external movements could be performed. The left pupil was larger than the right. There was no reaction to light, and that on attempting convergence and distant regard was defective. The sensibility of the cornea and the reflex

<sup>9</sup> Arch. Schlav. de biol., Paris, 1887, tome iii, 332.

<sup>10</sup> Trav. du lab. de Marey, 1880, tome iv.

<sup>11</sup> See Vincent, Thèse de Paris, 1910.

<sup>12</sup> See Souques, Soc. de neurol., May, 1905.

lacrymal secretion were present. Bilateral nystagmoid movements occurred.

Thus, there was complete paralysis of all the acts governed by the third nerve, with the exception of the pupillary reaction upon accommodation, convergence, and distance. Respiration was more rapid than normal—28 per minute. It was interrupted by paroxysms, especially after excitement. During these, breathlessness and angosise appeared, a "whooping" cough distressed her, the face reddened, and there was often abundant secretion of tears and saliva.

Phonation was rough, bitonal, nasal, and often almost inaudible. The right vocal cord was paralyzed, and the right side of the tongue was atrophied, corrugated, and showed fibrillary twitchings. There was, perhaps, a little facial asymmetry. There were no basal crises nor bulbar trouble other than the foregoing. However, it was a typical case of basal tabes as regards the cranial symptoms.

There were no tabetic symptoms in the lower limbs, but the deep reflexes were exaggerated, and the toes sometimes extended when stroking the sole. There were occasional lightning pains, but no visceral incontinences, and no other trouble of the nervous functions. Lumbar puncture showed an intense lymphocytosis. The diagnosis was clearly basilar meningitis, superior tabes.

During the two years which elapsed before her death few new symptoms appeared. The Jacksonian epilepsy reappeared. It was probably due to an area of cerebral softening found post mortem in the right hemisphere. The ocular palsies improved, although she never succeeded in convergence or holding the eye for more than an instant toward the inner canthus. The atrophy of the tongue, however, persisted.

At the *autopsy* the meninges did not appear diseased, and the cranial nerves seemed unaltered in volume, except the optic nerve, which had shrunk to about the size of a normal oculomotor. The right angular gyrus showed an old softening about the size of a quarter. Under the microscope the spinal cord revealed no degeneration of the posterior roots nor of the posterior columns, where the internal bandalette was quite intact. The anterior roots were also normal.

The optic nerve showed characteristic tabetic atrophy, not a single nerve fiber being preserved. The connective tissue presented a very severe endoneuritis and perineuritis, with arteritis of the type described by Marie and Leri,<sup>13</sup> and due to transverse "radiculitis" (the optic nerve is not a homologue of a spinal root); there was no lesion of the brain or eye to account for it.

*Oculomotor Nerves.* The lesions (Fig. 1) were nearly identical on the two sides. That of the left shows, 4 mm. after entering the

parietes of the cavernous sinus (Figs. 2 and 3), a distinct focus of transverse radicular neuritis. This is shown by the hypertrophy of the nerve (Figs. 4 and 5), but above all by the presence in its interior of vast bands of fibrous tissue, which dissociated and left only a few intact fasciculi (Figs. 6 and 7). Farther down it is not so intense, and it has disappeared 5.5 mm. after the entry of the nerve into the sinus. Thus, its length is only 1.5 mm. It corresponds to the spot just behind the place where the nerve is divided into compartments by the layer of connective tissue which accompanies its anastomotic branches.

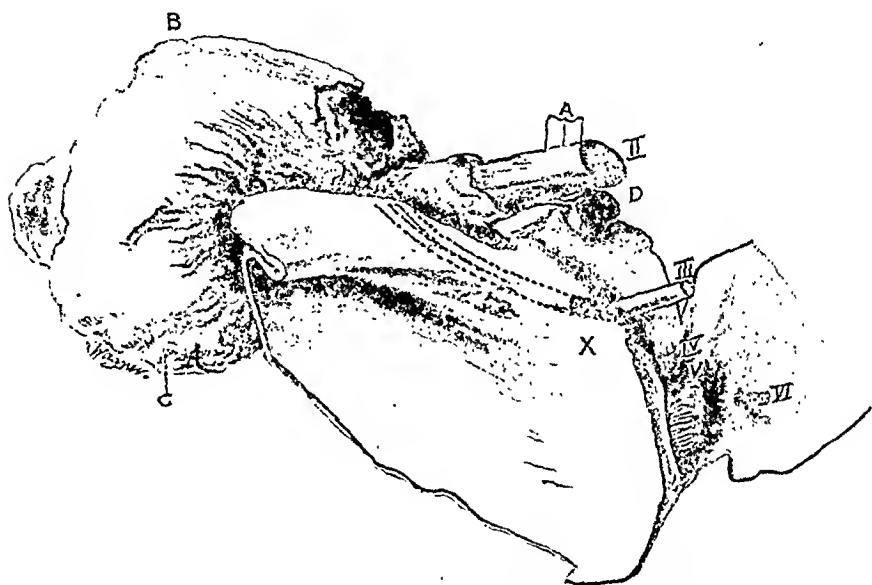


FIG. 1.—Meninges, globe of the eye, and cranial nerves removed intact to prevent tearing of the meningeal sheaths from the oculomotor nerve. The position and extent of the lesion is shown by the shaded area of the letter X. The subdural course of the oculomotor nerve is indicated by the dotted lines. A, three lines showing the direction in which the sections were made; B, globe of the eye; C, periocular fat concealing the nerves and muscles; D, internal carotid artery; II, optic nerve; III, oculomotor nerve; IV, pathetic nerve; V, trigeminal root; VI, abducens nerve.

At the parting the normal nerve becomes divided into compartments by the connective tissue, which, in a few millimeters, disappears. This is the spot where the endoneuritis has occurred. A little higher up one sees the line of the subarachnoid inflammation, now absorbed. The thickened vessel and the tucks of fibrous tissue indicate this. That the inflammatory process has not quite subsided is shown with hematein-eosin-orange stain (see original memoir). This shows that the nerve is still crammed with nuclei, and that the neighboring meninges are much altered, even obliterated, endoneuritis appearing, and that the inflammation is still present outside the sheath of the nerve, with the characteristic lymphocytes and, above all, plasma cells with the perinuclear halo. Thus it is clear

that we have over both third nerves the cicatrix of an old inflammatory focus of localized interstitial neuritis.

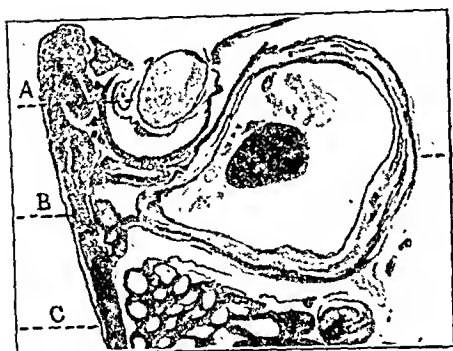


FIG. 2



FIG. 3



FIG. 4



FIG. 5

FIG. 2.—Transverse section (diagrammatic) of the region shown in Fig. 1, the section being made through the cavernous sinus proximal to the mark X. It shows the oculomotor nerve, A, lying in its meningeal gutter in the root of the sinus. There is at this situation no visible arachnoiditis. B, situation of the fourth and sixth cranial nerves; C, situation of the ophthalmic branch of the fifth nerve; D, internal carotid artery.

FIG. 3.—The third nerve, A, is now completely surrounded by its canal of dura and arachnoid matter, which are not yet adherent. The trabeculae of endoneuritis are visible; other structures are as in Fig. 2.

FIG. 4.—The inflamed arachnoid is shown adhering to the third nerve at one place. The endoneuritis is still more evident than in Fig. 3. Note the increase in volume of the nerve.

FIG. 5.—The third nerve is shown transversely and disassociated by thick trabeculae of connective tissue. Note the enormous increase in diameter of the nerve as against Figs. 2, 3, and 4, which are drawn to the same scale. The increased volume is due to the fibrinoplastic exudate and the round-cell infiltration within the sheath.

*The Nerve Fibers* (Figs. 8 and 9). The Weigert method shows the paleness of some of the nerve fibers among the dark violet of those remaining normal. Osmic acid shows the dwarfed and pale fibers, as in the preceding case,<sup>14</sup> but, above all, it reveals islands of regeneration. Both above and below the site of the lesion these islands are quite abundant, so that under low power the nerve

<sup>14</sup> Med. Record, January 29, 1910.

might be thought normal; but a higher power shows that the fibers they contain are often very small, squeezed together, without any connective tissue intervening. Serial sections show that they have come from a single nerve fiber, which buds out and follows an old neurilemma tract. They are significant of the presence of a noxa

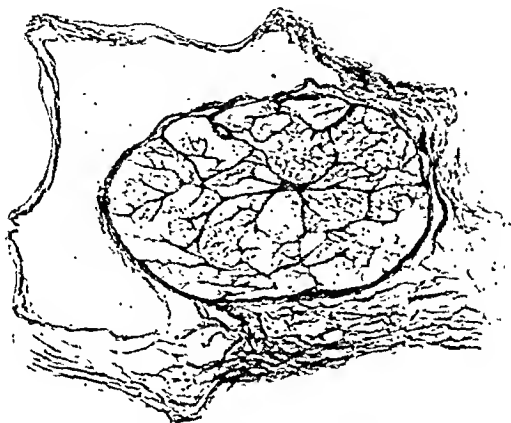


FIG. 6.—A microscopic view of Fig. 3, a transverse section of the oculomotor nerve near the commencement of the lesion. Note the endoneurial trabeculae of connective tissue and that only half the surrounding arachnoid is adherent. (Van Gieson stain.)

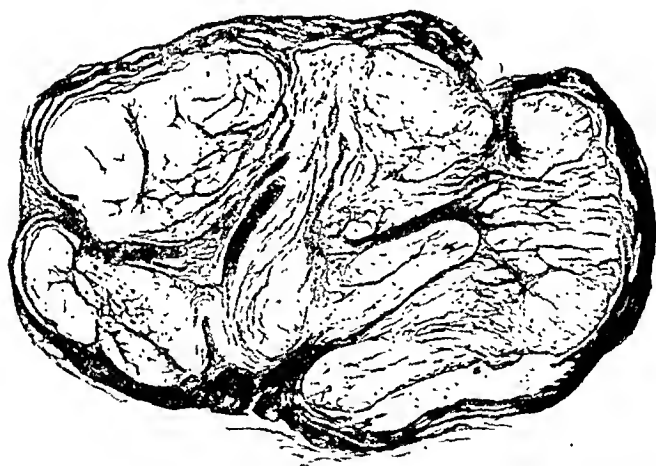


FIG. 7.—A microscopic view of Fig. 5, showing enormous neoformative endoneuritis, causing great enlargement of the nerve.

in some part of the course of the nerve, and they explain the manner in which certain tabetic palsies so much improve. In this case they are seen throughout the whole of the periphery of the nerve, especially in the fine branches penetrating the muscles, where their separation of the branches renders their study easier.

The hypoglossal nerve of this case shows changes in the nerve

fiber similar to those of a previous case,<sup>15</sup> and to those of the third, in that its nucleus was untouched. It is this which accounts for the absence of muscular atrophy in these cases. The nuclei of none of the cranial nerves showed any alteration, although carefully studied in serial sections; so that we may conclude that in this a focus of interstitial neuritis was the cause of the tabetic symptoms.

FIG. 9



FIG. 8

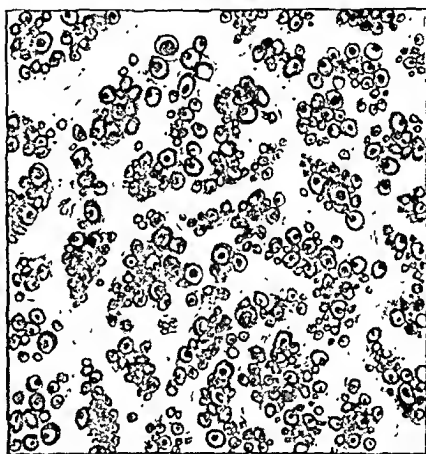
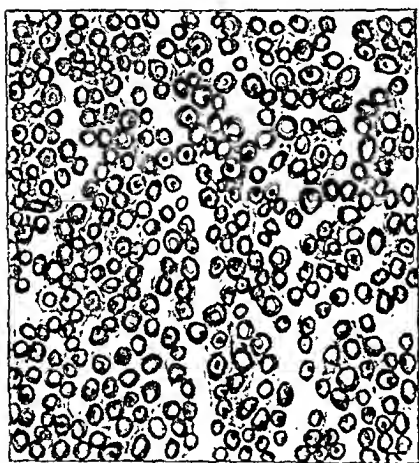


FIG. 8.—Transverse section of a normal oculomotor nerve. Note that the myelin rings and axis cylinders do not differ markedly in calibre.

FIG. 9.—The oculomotor nerve of the case studied (Azoulay method). Note the numerous atrophied fibres, small and pale, and their separation into groups by a proliferating endoneuritis. Some regenerating fibres are seen. (Low and high power magnification.)

Although even this intense lesion had not completely destroyed the functional efficiency of the nerve fibers, except the optic ones, yet it is conceivable that such destruction may, and indeed must, occur, as is shown by the lingual hemiatrophy of this case, and the fascicular palsy and reactions of degeneration of the muscle found in tabetics in varying proportions.

**PATHOLOGY OF FUGITIVE PARESIS.** Now, although this case does not explain the genesis of the Argyll-Robertson pupil; it does furnish the missing link in the chain of evidence required

<sup>15</sup> Lot. cit.

to explain the fugitive palsies of the ocular muscles which so often occur in the course of tabes. For, though in this case the palsies were persistent, another series of facts makes it clear why they are not so in all cases. For example, Vincent<sup>16</sup> examined another case of tabes with only mild cranial nerve symptoms in which, unfortunately, the oculomotor nerves were spoiled at the postmortem, but in which the hypoglossal, which is also an anterior root homologue, showed the commencement of changes as a result of the progress of which the appearances in our present case ensue. Although no clinical symptoms had appeared, in spite of a considerable endoneuritis and loss of quite a large number of fibers in the hypoglossal, yet this is easily accounted for by the wide distribution among the tongue muscles of each fasciculus of the twelfth nerve, so that each part of the tongue has retained at least some muscle fibers, of which the innervation persists, to enable the tongue to perform its movements without apparent impairment.

Very different is the result when only a few nerve fibers supplying an oculomotor nerve are attacked. A very slight diminution of the innervation conveyed, for example, by the sixth nerve to the abducens muscle interferes with the delicate muscle balance needed for the adjustment of the optic axes in binocular vision. Hence the derangement is at once manifested clinically as a paralytic diplopia. The thinness of the abducens nerve makes it particularly liable to implication in the inflammatory process of the leptomeninges as it traverses its long course at the base of the brain.

Why, then, does the paralysis usually clear up in a few days, unlike the present case?

THE PARESIS OF SECONDARY SYPHILIS. This question is answered by another series of facts, more especially conspicuous in what has been called the secondary stage of syphilitic affection. It is now known that even in this stage the meninges are inflamed quite often;<sup>17</sup> Buttino<sup>18</sup> believes in 40 per cent. of cases.

In addition to the general symptoms, such as headache, exaggerated reflexes, hyperirritability, and sometimes even Kernig's sign, quite a number of cases exhibit focal symptoms, such as facial paresis, local vasomotor changes, and neuralgias.<sup>19</sup> It is the rule for these to clear up along with the meningism, sometimes even without treatment. This only conforms to the tendency of the processes of lues venerea to resolve like those of other infective diseases.

THE CONTINUITY WITH THE TERTIARY STAGE. It has been supposed that the tertiary lesions differ in this respect, but it is becoming evident that no distinction of kind really exists between the periods of syphilis; for, on the one hand, some cases pass

<sup>16</sup> *Loc. cit.*

<sup>17</sup> Ravaut, *Méd. Soc. des Hôp. de Paris*, 1901, etc.

<sup>18</sup> *Riv. di Pat. Nerv. e. Ment.*, 1906.

<sup>19</sup> Drouet, *Thèse de Paris*, 1904.

to rapid paralysis and death within a few months,<sup>20</sup> while others show spontaneous recrudescence of symptoms<sup>21</sup> even many years after infection. Furthermore, Vincent's<sup>22</sup> examination of the cerebrospinal fluid of apparently healthy individuals having had syphilis has revealed, in several cases, an abundant lymphocytosis, and in some of these cases symptoms of tertiary syphilis of the nervous system showed themselves some months after his examination. It is clear, then, that between the secondary and tertiary stages of syphilis there is no absolute pathological or clinical differentium, as regards the nervous system at least; in either stage the lesions may be absorbed, and the structures involved may resume their function if they are not destroyed by the inflammation of the arachnoid, which is the fundamental lesion of tabes dorsalis.

**WHY RETURN OF FUNCTIONAL CAPACITY DIFFERS IN MOTOR AND SENSORY LOSSES OF TABETICS.** As regards the fibers emanating from the spinal and cranial ganglia, a destruction is definitive, for the secondarily degenerated fibers within the central nervous system cannot reintegrate, nor are the regenerated fibers within the roots capable of utilizing the anlage of a former course; hence sensory losses of tabetics persist in spite of resolution of lesions.

**THE ROLL OF EXERCISES.** The return of functional capacity acquired by what is known as the Fraenkel exercises is not due to the reestablishment of old nerve paths, or the establishment of new channels of afferent information, as is so often supposed; but it is due to the patient learning volitionally to utilize the imperfect afferent information, which is all that remains to him, and to create from it a new set of automatisms to replace those which now functionate in so disorderly a fashion as to create ataxia. But when resolution occurs in the inflammatory focus surrounding peripheral efferent fibers, the functional efficiency of the diseased nerves may be resumed, even though destruction of the nerve fibers has been complete. The reason is that the degeneration of an efferent neuron attacked while traversing the meninges is entirely peripheral; and, as we know, peripheral neurons can regenerate completely and resume their accustomed path as long as there is no mechanical interruption in the course of the growing fiber. A granulomatous cicatrix sometimes furnishes this obstacle, and then the loss of function is permanent, as in the present case.

**OTHER CAUSES OF NEURAL SYPHILIS, NOT TABETIC INTOXICATIVE.** As regards the genesis in anterior radiculitis of the muscular atrophies of tabetics, some recent pathological examinations have

<sup>20</sup> See case of Sicard et Roussy (*Rev. de neur.*, 1904), in which death occurred from acute meningitis seven months after the chancre, and post mortem intense subarachnoid infiltration, periarteritis, and endarteritis obliterans were found.

<sup>21</sup> Ballet and Barb., *Rev. neur.*, 1908.

<sup>22</sup> See author's article in *Med. Rec.*, January 29, 1910., and Vincent, *loc. cit.*



been used as arguments against the conceptions here presented, and in support of the dystrophic explanation of tabes dorsalis. Such, for example, are the cases of polyomyelitis antérieur chronique in syphilitics of Pierre Marie, Jr.,<sup>23</sup> and of S. A. K. Wilson,<sup>24</sup> which their authors attribute to a slow intoxication of the neurons, for, in Wilson's cases, he did not believe that the vascular changes were sufficient to account for the destruction of the anterior horn cells which he found. Leri's<sup>25</sup> observations on the same disease showed how often syphilis had been an antecedent; but, when it is remembered that there was a meningitis in all of Nageotte's cases, and that there was no disease of the gray matter in them, it is not difficult to see that Marie and Wilson are dealing with quite a different condition, which, though a chronic syphilitic one, may be of the same kind as the more acute and grave syphilitic intoxications revealed by the cases of Preobraschensky,<sup>26</sup> in which death rapidly ensued, and post mortem no sclerosis nor degeneration was found, but merely atrophy of the anterior horn and roots near the cord, along with infiltration of the vessels.

The case of Crouzon and Villaret,<sup>27</sup> too, was believed to be intoxicative, as, after some months of meningomyelitic sciatica, an acutely ingravescent ascending paralysis caused death in eight days in a man of forty-two. Again, in an ape, which died seven months after inoculation with *Treponema pallidum*, having been blind and ataxic for a month, Schroeder<sup>28</sup> found, post mortem, no round-cell infiltration, although the myelin of the optic nerve was entirely replaced by granules, and there was intense degeneration of the posterior columns. The ape's pupils had not ceased to react to light, and the tendon jerks had been exaggerated; Schroeder did not regard it as a case of true tabes, but of an acute intoxication. The role of the syphilitic vascular diseases in producing sclerosis of the spinal cord must not be forgotten either. Tabetics are no more immune to vascular disease of the spinal cord than other syphilitics. This is only in harmony with the frequency with which tabes and aortic disease occur together, as Babinski<sup>29</sup> pointed out long ago.

**VASCULAR CHANGES.** But there is another factor in the production of the sclerosis of the cord sometimes found in tabetics in addition to the pseudosclerosed appearance of the posterior columns produced by the secondary degeneration ensuing upon radiculitis. I refer to the perivascular infiltrations in the septa, extending into the cord from the inflamed pia mater, which have been described by Bently,<sup>30</sup> Paviot,<sup>31</sup> and Schroeder.<sup>32</sup> The latter found them in the brain stem

<sup>23</sup> Rev. neurol., 1909.

<sup>25</sup> Rev. neurol., 1907.

<sup>27</sup> Review of Neurology and Psychiatry, 1908.

<sup>29</sup> Rev. neurol.

<sup>31</sup> Soc. de Méd. des Hôp. de Lyon, 1905.

<sup>32</sup> Centralbl. f. Nervenkrankheiten u. Psychiat., 1907.

<sup>24</sup> Review of Neurology and Psychiatry, 1909.

<sup>26</sup> Neurol. Centralbl., 1908.

<sup>28</sup> Arch. f. Psych., 1908.

<sup>30</sup> See Beutler, Thèse de Lyon, 06.

and optic nerve as well, though not in the cortex of the five cases he examined and they did not occur in alcoholic pseudotabes. It is the same trabecular infiltration which is found in the cortex of paretics (Alzheimer<sup>33</sup>), but in tabes it is relatively rare, even though the pia is always thickened (Spiller<sup>34</sup>).

I have thought it right to mention these exceptional cases, so that the main issue should not be confused by a consideration of cases complicated by lesions of which the genesis differs so markedly from those of true tabes dorsalis. In this way the uninformed will not be deceived by criticisms of the radicular genesis of tabes; for they will know that criticisms of the nature indicated are founded upon epiphenomena which may occur in any syphilitic; although they could not be adduced with regard to the case here cited, yet they might be so adduced regarding some future case in which the cranial nerve paralysis of a tabetic was due to toxemia, arteritis, or nuclear disease. This would not be a cranial nerve tabes, for that disease, like the spinal tabes itself, is always due to the transverse radiculitis of Nageotte, whether this affects the sensory or the motor roots.

## ACUTE PULMONARY ŒDEMA AS A TERMINAL EVENT IN CERTAIN FORMS OF EPILEPSY.

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At the time the observations now to be narrated were made, that is, during the period of my active connection with the Ohio Hospital for Epileptics, from 1897 to 1905, and my then close touch with the literature of epilepsy, I could find no record to indicate that the syndrome, acute pulmonary œdema, epileptic seizures, status epilepticus, and sudden death in epileptics had been recognized. My purpose was to make it the subject of a special report, and brief mention of the matter was made in several communications<sup>1</sup> of that period dealing more or less fully with the question of status lymphaticus and its relation to epilepsy.<sup>2</sup> So far as I have been able to determine, it has received no general recognition to the present time. I wish, then, to invite attention to the subject of acute œdema of the lungs as a terminal event in certain forms of

<sup>33</sup> Ein Beitrag zur Histopath. d. Tabes Dorsalis, 1905, etc.

<sup>34</sup> Philadelphia Neurological Society, 1908.

<sup>1</sup> See A Consideration of the Neuroses of Status Lymphaticus, *Journal of the American Medical Association*, February 13, 1904; and the article Status Lymphaticus, *Reference Handbook of the Medical Sciences*, p. 453.

<sup>2</sup> See especially the *Bulletin of the Ohio Hospital for Epileptics*, 1898, vol. i, No. 1; 1898, vol. i, Nos. 2 and 3; 1904, vol. ii, No. 1.

epilepsy, and by the phrase "certain forms" to refer especially to that type of epilepsy in which status lymphaticus is found in morbid anatomical association.

Acute œdema of the lungs, even apart from any relation to epilepsy, is an uncommonly discussed clinical event, as one may judge from a recent excellent review by Riesman<sup>3</sup> who notes that little or no mention of it is made in the standard treatises on the practice of medicine. Besides carefully compiling the literature on the subject, Riesman describes the history of six personally observed cases of acute pulmonary œdema, but nowhere in his study does he mention its association with epilepsy, nor with status lymphaticus. In Geysen's thorough thesis<sup>4</sup> devoted to sudden death in epileptics, no allusion is made to fatal pulmonary œdema nor to status lymphaticus.

The acute serous inundation of the lungs has been observed in epileptics under several types—as accompanying a single major fit with death soon succeeding; after a single attack with coma, and death in a longer interval; after a series of fits not reaching status epilepticus; and as hastening status epilepticus to a lethal termination. There is also evidence, so far as postmortem observations go, that some of the not uncommon nocturnal fatalities among epileptics (the "found-dead-in-bed" class of institutional records) in reality are instances of acute pulmonary œdema after one or more epileptic attacks, rather than of mechanical asphyxia by bedclothing or otherwise, as is commonly believed.

To illustrate the variations just alluded to, typical cases have been selected from my notes, and will be described as concisely as possible.

CASE I.—The first patient was Jenny G., who was admitted to the Ohio Hospital for Epileptics in 1896, in her nineteenth year of age. Both grand mal and petit mal had existed since her seventeenth year. There were seldom more than one or two epileptic crises during a period of twenty-four hours; but a month rarely passed without at least one major attack. She was sane, and above the average epileptic inmate in intelligence, and her general health was good.

The woman had been in her usual health April 8, 1899; that evening she was in a cheerful mood, and spent some time in the attendant's room with several other inmates. At 8 P.M. she retired, and in half an hour had a severe major epileptic attack. Frothy, reddish mucus issued from her mouth during the convulsion and reappeared as it was wiped away. A comatose condition succeeded the clonic convulsions. She was seen by the physician shortly after the fit began, and was then lying on her back; the loud, stertorous

<sup>3</sup> Acute Pulmonary Œdema, with Special Reference to a Recurrent Form, *AMER. JOUR. MED. SCI.*, January, 1907.

<sup>4</sup> De la mort inopinée ou rapide chez les epileptiques. Thèse No. 1114, Faculté de Médecine et de Pharmacie de Lyon, 1895.

breathing with occasional attempts at coughing could be heard across the large dormitory; a thin, foamy fluid escaped from the mouth and nose; at times this fluid was pinkish, and when the woman was turned on her side a gush amounting to about two ounces would follow. After several of these passive movements it was found that they only further embarrassed breathing, and she was allowed to lie on her back. There was no cessation to the appearance of the foam and the occasional gushes of fluid. The respirations during this period were sixteen to twenty a minute, and coarse rales were plainly audible at a distance from the chest. The skin was cold and clammy; the pulse of good volume and only moderately accelerated. Toward the end breathing became as short gasps, and the pulse rapid and weak. Death took place at 10 P.M., one and one-half hours after the single epileptic attack.

*Autopsy.* The morbid anatomical findings of chief interest relate to the lungs and the anomalies of status lymphaticus. A pronounced diffuse oedema of the lungs was indicated before the removal of these viscera by the escape of voluminous gushes of thin, frothy fluid whenever the corpse was moved, and after their removal by a very heavy, boggy, waterlogged state, the free flow of bubbly serum when they were incised, and the weight (1820 grams) of both lungs. The thymus was large, fleshy, reached the level of the second rib, the seat of numerous punctate hemorrhages, 1 cm. in thickness, weighed 30 grams, and made up of closely set adenoid follicles. There was moderate enlargement of the superficial regional lymph glands, while those of the peritoneal cavity were generally large, soft, and pinkish in hue. The solitary follicles of the stomach and intestines were prominent, and so were Peyer's patches. The spleen was large (340 grams), but its follicles were not strikingly prominent. The thyroid was soft, pale, and about one-third larger than normal. There were no other visceral morbid changes.

CASE II.—Frank S., aged twenty-two years, was a victim of grand mal and beginning epileptic dementia. He was subject to periodic major attacks of much severity. The evening of March 8, 1899, he had returned to his cottage after partaking of a hearty supper in the central dining room, seemingly in his usual general good health. While standing in the main room with some companions he was suddenly seized with a fit and fell backward, forcibly striking his head on the floor. It was noticed at once that he had not breathed properly after the convulsive phase of the attack ceased, and when the physician reached the scene he found a condition of urgent dyspnoea, with frothy fluid escaping from the mouth. The coma continued, breathing became more labored, and in twenty minutes after the epileptic attack the patient expired.

*Autopsy.* As disclosed by the postmortem examination, a right-sided subdural hematoma with a bulk of 50 c.c., without demon-

strable fracture of the bone or rupture of meningeal bloodvessels, had resulted from the fall. Foamy, blood-stained fluid covered the lips, cheeks, and nostrils, and when pressure was applied to the chest this fluid freely gushed from the mouth and nose. The lungs distended the pleural cavities, were boggy, and exuded bloody, frothy fluid during their manipulation, both before and after incision. A diffuse, reddish, oedematous infiltration appeared on section, the extent of which can be judged by the combined weight (2170 grams) of the freshly removed lungs. The thymus was quite large, bilobed, reddish in color, and of compact adenoid tissue; the tonsils were large, projecting so as almost to touch in the middle line. The superficial, bronchial, and mesenteric lymph glands were larger than ordinary. The spleen weighed 290 grams, and its follicles were large and prominent in the red pulp. The lymphoid follicles of the whole digestive tract were very prominent.

CASE III.—James B. was twenty-seven years old when death occurred. His grand mal began when fourteen or fifteen years of age; gradual dementia supervened, with periods of religious mania, between which the man was a quiet, mild, and tractable patient. There was no unusual preliminary to the several fits that resulted fatally. The patient had retired for the night, July 5, 1900, as well as usual. He had several epileptic seizures before midnight, but as nocturnal attacks were not uncommon with him, the night attendant felt no alarm. At about 3 A.M. he had a severe general convulsion, and his breathing was so difficult and peculiar that the attendant sent for the physician, upon whose arrival breathing became easier, though coarse rales could be heard from both lungs. The pulse was good at this moment. As the attendant and physician looked on, another hard fit occurred, with foamy fluid gushing from the mouth, and in this condition breathing quickly ceased and life was extinct.

*Autopsy.* Thin, frothy, blood-stained fluid escaped from the mouth whenever the body was moved. Both lungs were voluminous, adherent behind and laterally; oedematous fluid escaped from the incisions. They weighed 1050 grams. The thymus was thick, fleshy, with solid thymic adenoid follicles, and beset with hemorrhagic foci. The other features of status lymphaticus were enlarged and prominent intestinal and splenic follicles.

CASE IV.—Effie P., aged 20 years, sane; occasional grand mal; had been debilitated for some time. During the night of March 3, 1901, she had four severe fits; for the three succeeding days she acted queerly, was confused, but went to meals regularly. The next day a distinctly disturbed state set in, with constant incoherent talk, efforts to remove clothing and a generally dazed condition—epileptic mania. Sleep was induced that night by large doses of paraldehyde, and the following day a quiet, taciturn, sullen mental state developed. The patient went to her dinner and ate a moderate meal, but at 2. P.M. the fits again began, and by 7 P.M. her temper-

ature was 98°, pulse 130, respirations 42; the woman was unconscious, lips cyanotic, and gurgling rales could be heard to emphasize the labored breathing. At this hour three attacks were noted by the physician, and after each one considerable frothy fluid issued from the mouth. The gurgling continued, with frothing at the mouth; two more fits were recorded before 1.30 A.M., when death occurred.

*Autopsy.* The findings were essentially as have been described in the preceding cases. The lungs were free in the pleural cavity, boggy and œdematous, and weighed 1230 grams. The anatomical features of status lymphaticus corresponded to those already described.

CASE V.—Arthur A., aged twenty-five years, a victim of grand mal and epileptic dementia, began to decline. Thinking the condition due to bromism, the drug was suspended. The epileptic attacks at once became more frequent, from three to five each day. About four weeks after discontinuing the bromides, a series of grand mal began toward the morning of March 11, 1901; by 10 A.M. there had been fifteen attacks. Bromides were pushed without avail. At 11 A.M. consciousness was lost and a temperature of 102° was noted; fits occurred every fifteen to thirty minutes until 5 P.M., when death ensued in the midst of a general severe convulsion which terminated the status epilepticus. Marked dyspnœa had been noted about half an hour before the end.

*Autopsy.* A moderate œdema of the lungs was disclosed, together with a picture characteristic of status lymphaticus.

So much for this hurried review, in which I have endeavored, by citing the salient clinical and pathological points in five typical cases, to illustrate my thesis. In passing let it be understood that the thorough investigation at autopsy precluded the existence of renal, cardiac, or cerebral disease as explaining the causation of the pulmonary œdema; and further, that in each case a negative result followed the search for foreign bodies in the air-passages, which might have induced a mechanical suffocation.

As to the relative frequency of pulmonary œdema in epileptics, the following statistics from the records of the Ohio Hospital for Epileptics will bear witness. In the years 1903, 1904, and 1905 there were a total of 203 deaths; of these, 41 followed a single epileptic attack, or were otherwise sudden, as for example, nocturnal fatalities, in which the individual was found dead in bed. In this group of 41, œdema of the lungs was noted, either as a terminal clinical event, or was verified at autopsy in 13 cases. Again, in the period above mentioned 41 patients succumbed to status epilepticus, and among these œdema of the lungs was noted in 15 cases. That the syndrome, acute œdema of the lungs and epileptic attacks is truly a "terminal event" seems evident from the foregoing recital.

The full significance of acute pulmonary œdema in epilepsy is at most conjectural, but with what my studies have disclosed as to the

existence of status lymphaticus in these cases, we can suggestively recall the fact, repeatedly emphasized by those who have occupied themselves with that peculiar morbid condition, viz., that a tendency to sudden and usually fatal œdema—as of the larynx, lungs or brain—is one of the outstanding peculiarities of the victims of the lymphatic constitution. Accordingly, the observations here recorded should tend in two directions—to emphasize the importance of acute œdema of the lungs as a concurrence in epilepsy, and further to illustrate the kinship between certain types of epilepsy and status lymphaticus.

## THE PHYSIOLOGICAL UTILIZATION OF SOME COMPLEX CARBOHYDRATES.

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It is still a current practice, especially among medical men, to look upon the proximate analysis of a food material as an adequate index of its nutritive value. In certain cases the data thus gained may be depended upon to give reliable information regarding food values; in others, however, the chemical statistics derived from the more familiar analytical procedures can become quite misleading. The explanation of this lies in the fact that much of the information furnished by the analyst is indirect in character. Protein is estimated on the basis of nitrogen content. This method may lead to erroneous conclusions in the case of plant products in particular, in which a diversity of nitrogenous constituents other than proteins are frequently present. The ether extract is designated as fats, although it is known frequently to contain lipoids, notably phosphatides, the real nutritive value of which is uncertain. The carbohydrates are not infrequently estimated by difference—a method which not only is subject to inherent error, but also fails to give any indication of the specific character of the substances represented.

An illustration of the illusory character of such analyses is afforded by the investigations of one of us upon mushrooms. These are highly prized in certain quarters because of a supposed richness in protein which is attested by a considerable content of nitrogen. Experimental studies have shown, however, that the latter is present in indigestible form, in part as nitrogenous celluloses; any representations of composition made on the basis of such analytical determinations as have just been reviewed are obviously misleading.

Turning to the most abundant nutrient group in the dietary, there are additional reasons why even an accurate identification of the carbohydrate nature of a food component is no guarantee of its nutritive value. Aside from the fact that oftentimes the individual nutrients are presented in the naturally occurring foods in a form which renders their alimentary utilization difficult on mechanical or physical grounds, numerous carbohydrates are *per se* indigestible. In the case of cellulose this has been distinctly appreciated. It has been one of the contributions of the more recent physiological investigations to emphasize, (1) the need of digestion of foodstuffs prior to their utilization, and (2) the *specific* action of enzymes in virtue of which they are selective, as it were, toward certain substrates. An illustration of these facts may be taken from the behavior of the different sugars. Cane sugar, for example, is not utilized by the organism unless it is inverted to the six-carbon sugars, dextrose and levulose. Since the alimentary tract is the only part of the body equipped to carry out this reaction, cane sugar is not readily utilized unless it is introduced enterally in the body. The specificity of the inverting enzymes is exemplified in the observations that not all disaccharide sugars are inverted, that is, digested, with equal ease by the digestive secretions; and in certain species of animals, or at definite stages of development, one or the other of the characteristic inverting enzymes may be wanting. One of us has shown this to be the case in the equipment of alimentary enzymes in the embryo as contrasted with later stages of growth. The fact that the saliva of certain animals, the dog and cat for example, is devoid of amylolytic power is likewise suggestive in this connection.

At various times attention has been directed to the introduction into wider use of a great variety of food products rich in carbohydrates, which differ especially from the more familiar types in containing in place of starches and sugars a diversity of less common carbohydrates, such as polysaccharides of galactose, mannose, pentose, methyl pentose, dextrose, etc. These are widely distributed in plants and have been heralded as suitable food preparations under varied circumstances of choice or necessity. Remembering that when a foreign carbohydrate succeeds in entering the organism proper there is no guarantee of its being retained for nutritive functions unless it has been digested and is presented in the form of a six-carbon sugar, it becomes necessary to apply the direct test of availability in the organism itself. Despite their absorption, glycogen, dextrin, starch, cane sugar, lactose, inulin, may all escape unchanged from the body unless they undergo preliminary digestion. When the actual utilization of such carbohydrates is determined by feeding trials, all the possible digestive agencies—enzymes and alimentary microorganisms—are given an opportunity to contribute toward the appropriate preparation of the food for assimilation.



The fate of a number of the carbohydrates and products containing them is already known. The starches and common sugars disappear almost completely from the alimentary tract in man, so that their "coefficient of availability" is very high. It has been shown that inulin, on the contrary, is not converted into sugar by saliva, pancreatic or intestinal extracts, although specific inulases are found in vegetable forms. Inulin can be converted into levulose by the free mineral acid of the gastric juice; and herein seems to lie its most effective opportunity for conversion to sugar in the alimentary tract. Obviously the recommendations for the dietetic use of Jerusalem artichokes or topinambur, rich in inulin, need to be subjected to experimental test. Such investigations as have been made speak against the value of these foods, despite the readiness with which they yield levulose in the laboratory. The favorable reports have emanated from observations on diabetic patients in whom ingestion of inulin has not induced any corresponding output of sugar. The error of interpretation, when the loss of the ingested carbohydrate among the undigested food residues in the feces is not taken into account, is obvious.

In another place one of us<sup>1</sup> has considered in greater detail some of the suggestions which have been made from time to time, and some of the current practices in regard to a diversity of unexamined carbohydrate-yielding foods. The algæ, fungi, lichens, and tree barks, as well as certain roots and tubers, are included among these. The United States Bureau of Fisheries has publicly urged that the large number of algæ "susceptible of being prepared as palatable and wholesome foods" should be given a thorough trial. Many of the genera of "sea weeds" widely used for food purposes in Japan and Hawaii are abundant on our coasts. We need only mention more familiar names, such as Iceland moss, Irish moss, dulse, laver, murlins, vegetable gelatin (agar-agar), salep, Hawaiian "limu," and Japanese "nori," to indicate the character of the materials referred to. For several years they have formed the subject of nutrition investigations in this laboratory. In the present communication the results of studies by Dr. Swartz on a series of typical products actually used in certain quarters will be reported briefly. A more detailed account with the protocols will be published elsewhere.

In one group of experiments the various products have been added to the diet of man and animals (dogs) and the utilization determined by a chemical examination of the feces. In every case, the behavior of the various carbohydrates toward enzymes (human saliva, malt and "taka" diastases, dog's pancreatic juice or pig's pancreatic extract, extracts of dog's intestines and pig's stomach), and typical bacteria (mixtures of soil and fecal bacteria, pure cultures of *Bacillus coli*, and other aërobæ commonly occurring in the

<sup>1</sup> Mendel, *Zentralblatt f. Stoffwechsel*, 1908, No. 17; *Trans. Amer. Gastro-enterological Society*, 1908.

alimentary tract, and of putrefactive anaërobes) has been investigated. The fate of the constituent carbohydrates when they are introduced into dogs parenterally—with avoidance of the alimentary tract—has also been considered.

The food materials were derived largely from marine algæ, and included, besides the familiar dulse and Irish moss of our own markets, a number of species popular in the Hawaiian Islands. These were obtained through the kindness of Miss Minnie Reed, science teacher in the Kamehameha Manual Training School, Honolulu. For experimental purposes, water extracts were made whenever possible, and seaweeds which yielded no soluble carbohydrates in this way were ground in toto, and cooked before feeding. For convenience, these preparations may be grouped, according to their chief carbohydrate constituents, as follows:

*Pentosans*: Dulse (*Rhodymenia palmata*), and the Hawaiian algæ, limu lipoa (*Haliseris pardalis*), limu eleele (*Enteromorpha intestinalis*), limu pahapaha (*Ulva lactuca*).

*Galactans*: Irish moss (*Chondrus crispus*) and the Hawaiian algæ, limu manaua (*Gracilaria coronopifolia*), limu huna (*Hypnæa nidifica*), limu akiaki (*Ahnfeldtia concinna*), limu naualoli (*Gymnogongrus*), and limu kohu (*Asparagopsis sanfordiana*).

*Mannan*: Salep.

*Levulan*: Sinistrin, from the bulbs of *Scilla maritima*, known as squills.

The marine algæ named above consist chiefly of pentosans and galactans, the former being largely insoluble in water; the latter, soluble, and gelatinous in character like agar-agar.

The resistance to digestive enzymes in experiments *in vitro*, was very marked; ordinary diastatic enzymes were uniformly ineffective. With artificial gastric juice and "taka" diastase, twenty-four hours' digestion resulted in slight hydrolysis in a few instances, but control experiments with 0.2 per cent. hydrochloric acid indicated that digestion with gastric juice was due to the acid present rather than the action of any enzymes.

Bacteriological investigations showed that the carbohydrates under consideration are not readily attacked by microorganisms, but differ greatly in their ultimate powers of resistance. The galactan-containing Irish moss remained unaltered, even after a month's subjection to various species of bacteria; on the other hand, the levulan, sinistrin, and the mannan of salep were in part converted to reducing sugar by similar treatment. In the case of the soluble pentosan of dulse, no hydrolysis was observed, but decomposition gradually took place. In order of diminishing resistance to bacteria, therefore, these hemicelluloses may be said to stand thus: galactans, pentosans, levulans, mannans.

These same typical carbohydrates, introduced parenterally (subcutaneously or intraperitoneally) into dogs, were promptly

excreted through the kidneys and recovered in the urine apparently unaltered, precisely as previous experience with undigested carbohydrates would lead us to expect. In our feeding experiments the percentage of carbohydrate recovered in the feces bears a striking relation to the degree of resistance exhibited toward bacterial action, especially in the trials with human subjects. This is hardly surprising, in view of the demonstrated inability of the digestive enzymes to hydrolyze these preparations *in vitro*, and of the animal organism to utilize them without intervention of the alimentary tract. The galactans, although administered in the form of attractive and palatable blanc mange or jellies, in moderate quantities, showed an average elimination in the feces of about 75 per cent., Irish moss proving the most completely indigestible of all preparations of this group. On the other hand, the mannan from salep and the pentosan from dulse disappeared almost completely from the human alimentary tract. Preparations in which the pentosans were of the type insoluble in water, namely, those of the three Hawaiian limu—lipoa, eleele, and pahapaha—were excreted to about 50 per cent. unchanged. The utilization was, therefore, greater than has been obtained in similar experiments in this laboratory with a substance of the dextran group, *Cetraria islandica*, of which over 75 per cent. was excreted. These results warn us against drawing sweeping conclusions as to the digestibility of hemicelluloses as a class; each type must receive special consideration. At the same time, it remains to be shown, by means of respiration experiments, to what extent those hemicelluloses which do disappear from the alimentary tract in large measure (as the mannan of salep) are a true source of energy for the organism, and to what extent they are simply decomposed by bacteria into products which play at most an insignificant part in metabolism.

It is impossible to attribute much nutritive value to the galactan extracts so highly valued as demulcents and substitutes for animal gelatin, when 75 per cent. may be promptly excreted; but they may have a useful function in the dietary of persons with a tendency to constipation, by their presence, and their power of retaining moisture, giving desirable bulk and texture to the feces. This effect has been noticeable in several experiments.

There is a further possibility that those carbohydrates which do disappear in large measure from the alimentary tract may serve as stimulants to intestinal secretory activity, and so play an important rôle. An increase in the bulk of the feces was noticeable in certain experiments in which the carbohydrate had almost entirely disappeared during its stay in the alimentary tract. Many of these modern products may deserve a place in the dietary in health or disease as food accessories. It is from this point of view, rather than because of their reputed nutrient value, that they should receive notice from the student of dietetics.

## REVIEWS.

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SEVEREST ANEMIAS: THEIR INFECTIVE NATURE, DIAGNOSIS, AND TREATMENT. By WILLIAM HUNTER, M.D., F.R.C.P. (Lond.), Physician and Lecturer on General Pathology and Morbid Anatomy, Charing Cross Hospital, London. Vol. I; pp. 226. London: Macmillan & Co., Ltd., 1909.

DR. HUNTER'S book on what he terms *Severest Anemias* is devoted to an exposition of his well-known and somewhat original views regarding what is commonly spoken of as pernicious anemia; the present volume is limited to an historical preface and a discussion of the etiology, nomenclature, and pathology of the disease. In brief, Dr. Hunter's opinion is that the disease is a well characterized specific infective disease of hemolytic nature localized in the alimentary tract; that in its etiology, long-standing sepsis, oral and gastric, plays an essential and important antecedent and concurrent part; anemia is but one of the symptoms, of which there are three others—glossitic and gastro-intestinal, hemolytic, and febrile and nervous—far more characteristic and due not to the anemia, but to the infective agencies underlying the disease. Disapproving of the term pernicious, he separates this so-called Addisonian (primary cryptogenetic) anemia, a specific infective disease, sharply from other types of severe or pernicious (Biermer's) anemia, which he believes may be due to other types of general sepsis; and all these types characterized as infective anemias, he differentiates from so-called non-infective anemias—that is, chlorosis and all the ordinary posthemorrhagic and other types of secondary anemia.

There is much to support the view that oral and gastro-intestinal derangement is a part, if not the cause, of pernicious anemia; and from analogy and other facts the so-called cryptogenetic form of the disease seems to be hemolytic in nature. Dr. Hunter brings to the support of his main thesis all available data, which he marshals well; but he iterates and reiterates a good deal—which neither adds to the attractiveness of the discussion, nor lends additional weight to the opinions so frequently expressed. If "pernicious" is not a good term, assuredly "severest" is not better; between "severe" and its superlative, "severest" there seems little choice; "severe" certainly does not minimize the seriousness of the diseased condition; and undoubtedly one can scarcely support the attempt

to differentiate between an Addisonian and a Biermer's anemia, this altogether aside from one's necessary disapproval of the continued use of such eponymic names. While Dr. Hunter's discussion of the anemias from the etiological and clinical standpoint has much to commend it, he misses a fine point when he minimizes the significance of a study of the morphological and other changes in the blood during life. It is perhaps worth while to mention also the fact that he regards the changes in the bone marrow as reparative, secondary to the hemolysis. The book unquestionably is a notable contribution to medicine, and a credit to the industry, patience, and persistence of the author; but it falls short of being convincing. However, we expect to read it again, and we commend it to the serious attention of the profession.

A. K.

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DARWIN AND MODERN SCIENCE. Edited by A. C. SEWARD, Professor of Botany in Cambridge University. Pp. 595; 4 illustrations. Cambridge, England: University Press, 1909.

THE volume in hand is made up of a series of twenty-eight essays commemorative of the centennial anniversary of the birth of Charles Darwin and the fiftieth of the publications of the *Origin of Species*; and is edited by Professor Seward for the Cambridge Philosophical Society and the University of Cambridge Press Syndicate. After a tabular epitome of Darwin's life and the dates of publication of his books, the volume is introduced by a letter from Sir Joseph Dalton Hooker. The essays composing the body of the volume were suggested and the writers invited to contribute with a view of in some measure indicating the great and widespread influence, which Darwin has exerted upon civilized man; and while naturally a large proportion have been written by English scientists, and particularly by Cambridge men, there are numerous continental writers represented and two of the essays emanate from this country. All are of the highest authority and their combined publication constitutes a noble "Festschrift" in memory of the great leader of scientific thought, honorable in the highest degree to the writers and to the Cambridge originators. It is manifestly impossible in the brief space of such an article as this to note in detail or even to comment upon each of the essays; nor can the character of such a volume be regarded open to critical review. Published in commendation of a man to whom the world must always be a debtor, the Cambridge University Press has agreed to turn over to the University any profits which may possibly accrue for the purpose of endowment of biological research.

Charles Darwin was perhaps of all those competent to judge most disposed to minimize the influence of his work upon subsequent scientific thought and methods. He marvelled at the rapid progress of science for which his own contributions furnished the greatest impetus; and it is doubtful if his modesty permitted him to recognize for his own credit even a fraction of the importance his life bore in that progress—a life which he said he had employed “in adding a little to Natural Science.” But while his work dealt primarily with matters within the strict limits of biology as commonly understood, geology, psychology, ethics and sociology, modern philosophy, philology, religion, and cosmology all bear witness in this volume to the influence which his work has brought forth; and within the conventional bounds of biology, the papers upon the selection theory by Weissmann, upon variation by de Vries, heredity and variation by Bateson, cellular structure and heredity by Strasburger, Haeckel’s Darwin as an anthropologist, his influence upon animal embryology by Sedgwick, the paleontological record of animals by Scott of Princeton University, and that of plants by Scott of London, upon the experimental study of the influence of environment upon animals by Jacques Loeb; of the University of California, as well as others in the group, bear ample evidence. New facts and new views have grown up since Darwin’s time. Darwin, in admiring comment to his friend and peer, Alfred Russell Wallace, speaks of their richness as consoling “for our efforts being overlaid and forgotten”—it is merely as the rocks of the foundation are overlaid and forgotten, but ever relied upon as the sustaining elements of the entire structure. How far this influence may reach today with its near approach to the appreciation of inheritance, its rational conception of man and his place in nature, its wider and wider application of scientific principles to human environment, its elimination of more and more of the superstitions in religion, points to a morrow of material improvement in human existence of a variable evolutionary perfection of the physical man, and to a psychological realization of his relations only dimly conceived of now. Whoever may have preceded Darwin and anticipated this or that idea of Darwin’s, none utilized them or placed them openly for use, as did he; and it must always be true as Osborn, of Columbia, said of him, that in science Darwin must stand as an epochal figure, before or after Darwin must be as *ante* or *post urbem conditam* was for the Roman calendar. The value of the volume for itself, both for the essays discussing the immediate work of Darwin in this or that biological field and fixing those bearing upon the more modern fruits of his influence widening out into the cognate branches, should attract a large sale; and, after Darwin’s own published works, it must rank among the highest of Darwiniana.

SELECTED PAPERS ON HYSTERIA AND OTHER PSYCHONEUROSES.  
By PROFESSOR SIGMUND FREUD, Vienna. Authorized Translation by A. A. BRILL, Ph.D., M.D., Clinical Assistant in the Department of Psychiatry and Neurology in Columbia University, New York. Pp. 200. New York: The Journal of Nervous and Mental Disease Publishing Company, 1909.

THIS is the fourth of the Monograph Series edited by the *Journal of Nervous and Mental Disease*. The subject matter is divided into ten chapters, and consists, as indicated by the title, not of a continuous text on one subject, but selected papers. The editors have done their work well, and the translator, A. A. Brill, still better, for anyone who has read the original can appreciate the difficulty of translation. A word might be said here in praise of Drs. Smith Ely Jelliffe and William A. White, who are the editors of this series. So far, four of the monographs have appeared, and the reviewer, who has had the opportunity to read all, can only express his personal appreciation. The subjects which have been selected have been well considered, and all neurologists should be indebted to these gentlemen for having brought within their easy reading such difficult subjects as the psychology of dementia præcox and Freud's views on hysteria.

It is rather difficult in a short review to discuss this work, for to do so intelligently it would be necessary to re-state Freud's views of hysteria and his method of psycho-analysis, which consists in its cure. He begins by tracing the origin of so-called hysterical phenomena, and calls attention to what has already been brought out, that the hysteric suffers mostly from reminiscences. He holds that the reason that these reminiscences recur is because at the time of the original insult there was not sufficient explanation for them, and that they will recur just so long as the original condition persists. To him, just as one can, for example, cause a trauma of a nerve, just so one can cause a traumatic condition of a thought. The effectual cure of one is the cure of the other, and this is the basis of his psycho-analysis. He cites two examples at length. In these he brings out his method of analysis and effectually demonstrates that when any mental impression which has been the basis of an hysterical thought is explained, corrected, and normally associated, a recurrence of that particular thought is impossible, because there is no remaining cause of irritation. It is impossible to go farther into this matter in a short review. There are excellent chapters on psychotherapy and hysterical fancies.

At this point it might not be amiss to say a few words regarding Christian Science, mental healing, osteopathy, and similar cults. What practitioner has not had many intelligent patients go to one of these and be helped? The question arises naturally as to the cause for their apparent success and the continuance of their propa-

ganda. One reason is that the average patient who comes to a physician, whether he be a general practitioner or specialist, and complains of a symptom which is usually regarded to be neurasthenic or hysterical, is either told to forget it or that nothing is the matter with him. But, as a matter of fact, does one convince the patient, whether intelligent or stupid, that he has no pain or that his symptom does not amount to anything, when he is suffering? And again, does the average physician tell the patient how to forget it? Not at all. He goes away from the physician's office probably encouraged for the time being, but when the pain comes back he is as badly off as ever. What happens to him when he goes to an osteopath or a Christian Scientist? The first will tell him that he has a dislocation of his vertebræ or a lesion somewhere, and that he needs twenty treatments at five dollars a visit, and assures him that he can cure him, and he goes at his patient and does something for him, which to the patient means more than being told to forget, but not being shown how, or that there is nothing the matter with him. If he goes to a Christian Scientist, the "Scientist" will probably do the same thing by getting the patient's thoughts away from himself by concentrating upon Mrs. Eddy or someone else, but the effectual thing is that something is being done. It is not a matter of argument that quite a number of patients are not helped by Christian Scientists and osteopaths. The important thing is that they do something for the patient.

It should not be gathered from the above that psycho-analysis is Christian Science, or that Christian Scientists employ psycho-analysis. Far from it, for the "Scientist" simply tells the patient that he will cure him of his symptoms, but makes no attempt at psycho-analysis, and he depends entirely upon suggestion to effect his cure, whereas, by psycho-analysis an hysterical thought is removed in a reasonable, logical, and concrete manner. T. H. W.

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PROGRESSIVE MEDICINE. A Quarterly Digest of Advances, Discoveries, and Improvements in the Medical and Surgical Sciences. Edited by HOBART AMORY HARE, M.D., Professor of Therapeutics and Materia Medica in the Jefferson Medical College, assisted by H. R. M. LANDIS, M.D., Demonstrator of Clinical Medicine in the Jefferson Medical College, Philadelphia. Vol. iv, pp. 334. Philadelphia and New York: Lea and Febiger, 1909.

VOLUME IV of *Progressive Medicine* for 1909 opens with an excellent discussion of recent advances in diseases of the digestive tract and allied organs, the liver, and the pancreas, by David L. Edsall. Particular attention is paid to œsophageal carcinoma,



cardiospasm, the Salomon test in diseases of the stomach, several forms of gastritis, achylia gastrica, dilatation of the stomach, gastric ulcer, gastric carcinoma, constipation, appendicitis, cirrhosis of the liver, pancreatitis, the Cammidge reaction, etc. J. Rose Bradford discusses diseases of the kidney, particularly the experimental production of nephritis, albuminuria, hematuria, the  $\alpha$ -rays and renal calculi, and calculous anuria. Joseph C. Bloodgood analyzes recent advances in the surgery of the extremities, shock, anesthesia, infections, fractures, dislocations, and tumors. William T. Belfield discusses genito-urinary diseases, especially gonococcic infection (local and general), colon-bacillus infection, decapsulation of the kidney, lavage of the renal pelvis and ureter, and diseases of the prostate and the bladder. H. R. M. Landis concludes with a valuable therapeutic referendium, in which he makes special mention of adrenalin, antidiphtheritic serum, antimeningitic serum, antitetanic serum, apomorphine, atoxyl, belladonna, Coley's toxins, digitalis, fresh air, iodine, lactic acid, magnesium sulphate, the nitrites, phenolphthalein, pituitary extract, venesection, etc. The publication continues to merit the professional attention and approbation bestowed upon the preceding volumes. A. K.

**EXPERIMENTAL RESEARCHES ON SPECIFIC THERAPEUTICS.** BY PAUL EHRLICH, M.D., Director of the Royal Institute for Experimental Therapy in Frankfort, Germany. Pp. 95. New York: Paul B. Hoeber, 1909.

**IMMUNITY AND SPECIFIC THERAPY.** BY W. D'ESTE EMERY, M.D., Clinical Pathologist to King's College Hospital, London. Pp. 448; 71 illustrations. New York: Paul B. Hoeber, 1909.

EHRLICH's little book comprises a reprint of his Harben Lectures for 1907, delivered upon invitation of the Royal Institute of Public Health of London. The lectures were devoted to immunity with special reference to the relation existing between the distribution and the action of antigens, to the atreptic function, and to chemotherapeutic studies on trypanosomes. Those not familiar with the subjects must assuredly become much informed by the deductions of a master mind, of one who has established certain principles that seem to underly a rational scientific therapy.

Emery's book, as the author states, comprises an attempt to give a connected and symmetrical outline of the chief facts definitely known with regard to the method in which the body protects itself against infections, and of their applications in the diagnosis, prevention, and treatment of disease. There is a full and complete discussion of the nature of toxins, of the phenomena of antitoxin

formation, of the interrelations of toxin and antitoxin, of the origin of antitoxin, of the side-chain theory, and of immunity to toxins, as well as of such subjects as agglutinins, precipitins, phagocytosis, reactions and similar phenomena, the colloidal theory of antibodies, and immunity to bacteria. A considerable part of the book is devoted to exemplifications of the practical application of specific therapy to divers sorts of infections—all of which is exceedingly well told and amply repays the reading. A. K.

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THE PRACTICE OF GYNECOLOGY. By WILLIAM EASTERLY ASHTON, M.D., LL.D., Professor of Gynecology in the Medico-Chirurgical College, Philadelphia. Fourth edition; pp. 1062; 1058 illustrations. Philadelphia and London: W. B. Saunders Company, 1909.

THE fact that this book has reached its fourth edition in as many years is a high tribute to its quality and the place it fills in the library of all interested in the field of gynecology. Compared with the previous edition, there are a few less pages of text and the same number of illustrations. Portions of a number of chapters have been rewritten and some extensively altered to give the reader the more recent views and methods of treatment in use today. Some of the most important changes made have been in the consideration of immediate versus the deferred operation in ectopic gestation, the treatment of peritonitis by the Murphy-Fowler method, the treatment of erysipelas of the vulva by the use of magnesium sulphate, the etiological factor that the modern dress, especially the modern corset, plays in the production of many of the pelvic diseases of women, and the influence of defective body form in the production of movable kidney. The book is very well illustrated throughout; the text is clear; the important parts in the text accentuated. The entire book is practical and instructive, and can be thoroughly commended to all workers in gynecology. J. A. K.

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MINOR AND OPERATIVE SURGERY, INCLUDING BANDAGING. By HENRY R. WHARTON, M.D., Surgeon to the Presbyterian Hospital, Philadelphia. Seventh edition; pp. 657; 555 illustrations. Philadelphia and New York: Lea & Febiger, 1909.

A REVIEW of Wharton's work on *Minor and Operative Surgery* appears almost needless, as it is so well known to the student and

practitioner. A few changes have been made in the present edition, consisting mainly of new text on Bier's hyperemic treatment, the addition of some recent minor surgical methods, and the description of a number of new operative procedures. All parts of the book have been thoroughly revised and a number of new illustrations added. Of these, may be mentioned those illustrating the use of adhesive plaster in the treatment of leg ulcers and in strapping the foot and lower leg for sprains of the ankle, and those illustrating the use of Bier's hyperemic methods. The book is a very valuable one on the subject, especially in view of the present-day tendency to overlook everything that is not major in surgery. J. A. K.

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DISEASES OF THE NOSE, THROAT, AND EAR. By WILLIAM LINCOLN BALLENGER, M.D., Professor of Otology, Rhinology, and Laryngology in the College of Physicians and Surgeons, Department of Medicine, University of Illinois. Second edition; pp. 932; 508 illustrations. Philadelphia and New York: Lea & Febiger, 1909.

THE second edition of Ballenger's book has been not only very greatly enlarged, but every page shows evidence of careful revision on the part of its author. In reviewing the first edition, a prediction was made that the book was destined to win a prominent place in the literature of diseases of the nose, throat, and ear. This prediction has been fully confirmed. In the process of revision, the different divisions of the work have been more carefully proportioned to one another, and the respective subjects of the diseases of the nose, throat, and ear are all of them now considered with a thoroughness and detail which fully justifies the author's statement in his preface, that the volume may be characterized as a "combined text-book and atlas, covering its three subjects." Dr. Ballenger's description of operative procedures are especially notable for their conciseness and lucidity, and the letter-press is accompanied by pictures which thoroughly illustrate all the details of the operation, which it is sometimes so difficult to render clear in the merely written description. Among the noteworthy additions, we would lay stress on the very excellent section devoted to an account of the functional tests of the ear. We know of no other text-book in which these recent advances in otological science are so well and thoroughly given. There is also a very good article on direct laryngoscopy and bronchoscopy. The work may be thoroughly commended as suitable for purposes not only of the student and practitioner, but also of the specialist, who desires a work of reference in which he may have access to the most recent advances in the subjects of which it treats.

F. R. P.

THE THEORY AND PRACTICE OF INFANT FEEDING, WITH NOTES ON DEVELOPMENT. By HENRY DWIGHT CHAPIN, A.M., M.D., Professor of Diseases of Children at the New York Post-Graduate School and Hospital; Attending Physician to the Post-Graduate, Willard Parker, and Riverside Hospitals. Third edition; pp. 350; 107 illustrations. New York: William Wood & Company, 1909.

A CAREFUL comparison of the third revised edition of Dr. Chapin's *Theory and Practice of Infant Feeding* with the original edition, which appeared in 1902, shows little change or modification in the text. The new edition contains some twenty-five pages more than the original, consisting largely of additions to the chapter on the milk of different animals, and the illustrations have been increased from 97 to 107.

Dr. Chapin's book stands for an authoritative exposition of the principles of top-milk feeding and the use of dextrinized cereal gruel diluents, with both of which subjects Dr. Chapin's name is identified. Cream and undermilk, or cream and whole milk mixtures, even when the cream is obtained as a definite percentage, and top-milk by the author's dipper receive little consideration, while the possibilities of whey as a diluent or as an ingredient of feeding mixtures, other than the so-called whey and cream mixtures, are dismissed with the statement that "the proteids of whey do not seem to have as much nutritive value as the proteids of the original milk from which it was made."

T. S. W.

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THE PRACTICE OF ANESTHETICS. By ROWLAND W. COLLUM, L.R.C.P. (Lond.), M.R.C.S. (Eng.), Anesthetist to St. Mary's Hospital, the Charing Cross Hospital, and the Hospital for Sick Children; and GENERAL SURGICAL TECHNIQUE, by H. M. W. GRAY, M.B., C.M. (Aberd.), F.R.C.S. (Edin.), Surgeon and Lecturer on Clinical Surgery, Royal Infirmary, Aberdeen. Edited by JAMES CANTLIE, M.A., M.B., C.M. (Aberd.), F.R.C.S. (Eng.), Surgeon Seamen's Hospital Society; Lecturer on Surgery in the London School of Tropical Medicine. Pp. 365; 103 illustrations. New York: William Wood & Co., 1909.

THIS volume, comprising No. 1 of a Medico-Chirurgical Series, is offered to the profession with the avowed purpose, as expressed by the editor, to present "the medical and surgical aspects of a disease, as well as the medical and surgical treatment, considered as a whole instead of in piece-meal fragments in separate volumes." Diseases requiring the coöperation of a physician and a surgeon in their pres-

entation will be treated by both in the writing of each volume. The book is divided into two portions: The first, treating of the practice of anesthetics, begins with a brief historical review of anesthesia, and then considers in detail the chemical properties and impurities of the various anesthetic compounds, the physiology of anesthesia, the preparation necessary in the administration of anesthetics, the selection of the various anesthetics, and methods of procedure in special cases and with the different anesthetics. The difficulties, dangers and their treatment, and the after-effects of the various agents are carefully detailed. This portion of the book is very thorough and instructive. The only adverse criticism that can be made is that the author practically ignores the open or drop method in the administration of ether which is extensively employed in the United States, and exception may be taken to the statement (p. 145) that, "In America, the Allis' inhaler is almost exclusively used."

In the second half of the book, treating of general surgical technique, special chapters are devoted to the preparation of the surgeon and his assistants, the care of the operating room, ligatures and sutures, bandaging, the preparation and after-treatment of patients, operations in private houses, and the common surgical operations which may have to be undertaken by the general practitioner. The book throughout is very well written, an undue amount of space is not given to unimportant details, and it can be highly recommended, not only to the general practitioner, but to the skilled anesthetist and general surgeon.

J. A. K.

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A MANUAL OF BACTERIOLOGY. By HERBERT U. WILLIAM, M.D., Professor of Pathology and Bacteriology in the University of Buffalo. Revised by B. MEADE BOLTON, M.D., Bacteriologist to the Bureau of Animal Industry, Washington, D. C. Fifth edition. Pp. 466; 113 illustrations. Philadelphia: P. Blakiston's Son & Co., 1909.

IN the new edition of William's well-known *Manual of Bacteriology*, Bolton has brought the book well abreast of the science as it is today. Many references, especially to the newest American literature, have been added. The subjects of diversion of the complement, trypanosomes, amœbæ, hygienic examination of milk and water, disinfection and surgical asepsis have been much changed and expanded. Here and throughout the book much important information is given in comparatively few and simple words. Dealing with the subject in a broad manner, written in clear concise English, accurate in statement, and representing the newest teaching practically along all lines of bacteriological research, the book will surely continue to be a very useful one to the student, teacher, and laboratory worker.

G. C. R.

MANUAL OF MILITARY HYGIENE FOR THE MILITARY SERVICES OF THE UNITED STATES. By VALERY HARVARD, M.D., Colonel, Medical Corps, United States Army; President of the Army Medical School, Washington, D. C. Pp. 481; 235 illustrations. New York: William Wood & Company, 1909.

THIS book has been written to present the art and science of military hygiene, especially as it has been evolved in our own army during the past few years. The treatise is intended to reach other branches of military service than the medical corps alone, and for this reason it is written in a simple, somewhat elementary style, and technical terms are avoided so far as possible. The book covers a large number of subjects in its thirty-nine chapters, and so, of course, the treatment of them is in part necessarily superficial. There are, however, many interesting groups of statistics gathered from the military medical records from the United States and foreign armies. The best part of the book seems to be that dealing with the hygiene of military construction, camp regulations, and sewage disposal. This book should be of much value in disseminating a wide-spread knowledge of rational, modern hygiene among the officers of our army, without which intelligent coöperation and therefore a perfect hygiene is practically impossible.

G. C. R.

ATLAS UND GRUNDRISS DER TOPOGRAPHISCHEN UND ANGEWANDTEN ANATOMIE. By DR. MED. OSKAR SCHULTZE, Professor of Anatomy in Würzburg. Second edition; pp. 224; 22 colored plates and 205 illustrations in the text, mostly in colors. Munich: J. F. Lehmann, 1909.

THIS first volume of Lehmann's *Medical Atlases* is one of the few German works on topographical anatomy which includes any reference to applied anatomy. The appearance of a second edition six years after the publication of the first is sufficient evidence that the volume has made friends among students of anatomy and operating surgeons. In the present edition the references to applied anatomy, which in the first edition were scattered here and there in the topographical sections, have been gathered together in separate paragraphs, and are, therefore, much more useful for reference. More than 115 illustrations have been added, drawn by Herr Hajek, who, in conjunction with Herr Schmitson, supplied those used in the first edition.

The volume treats, in order, of the head, neck, upper extremity, chest, abdomen, pelvis, and lower extremity; and a sufficiently complete index is added. Under each section the various regions

(shoulder, upper arm, elbow, forearm, wrist, etc.) are discussed in order, including under each heading short paragraphs, first on the topographical anatomy, and then remarks on applied anatomy. The topographical sections are not particularly noteworthy, and those dealing with applied anatomy fall far short of the ideal. The main value of the volume lies in its excellence as an atlas. Most of the colored plates are, we believe, so far unexcelled for beauty and clearness, as well as for accuracy in anatomical detail, albeit a few errors have been noticed. For instance, in Fig. 79 the medial head of the triceps appears as the direct continuation of the coraco-brachialis; Fig. 72 has two misprints in the "leaders;" Fig. 86 has another, etc.

The illustrations are fairly divided among the various sections, so that the volume is well balanced; but the vast majority of the figures appear to have been made from the point of view of topography, the applied anatomical illustrations being conspicuous by their scarcity. There are, moreover, no adequate illustrations of the brain, joints, stomach, prostate, or perineum. The new nomenclature is adopted throughout, but the old familiar terms are occasionally added in parentheses.

A. P. C. A.

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PRACTICAL DIETETICS. By W. GILMAN THOMPSON, M.D., Professor of Medicine in the Cornell University Medical College, New York. Fourth edition. Pp. 928. New York and London: D. Appleton & Co., 1909.

As the author says in his preface, the subject of foods and dietetics has made great advances since the first edition of *Practical Dietetics* in 1895. Each edition of this well-known work has been fully abreast of the subject, however, and this fourth edition is no exception. Foods and food preparations, stimulants and condiments, cooking of foods, and food digestion are all described. The relation of food to special diseases and a detailed discussion of food administration and dietetics in general, form the greater part of this excellent work. To make new comment on the book is as impossible as it would be futile, since, as some embryo author remarked after reading Shakespeare, "Nothing has been left unsaid."

E. H. G.

# PROGRESS OF MEDICAL SCIENCE.

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## MEDICINE.

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UNDER THE CHARGE OF  
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**Arteriosclerosis and Palpable Thickening of the Arterial Wall.**—FISCHER and SCHLAYER (*Deut. Archiv. f. klin. Med.*, 1909, xeviii, 164) publish the results of a clinical-anatomical study, undertaken for the purpose of determining the alterations in the arterial wall which render it palpable. Their material consisted of seventy-five arteries obtained from twenty different subjects. A comparison of the palpability of the artery and its anatomical condition showed that in one half of the cases in which, anatomically, there was sclerosis of the intima, no thickening of the artery was demonstrable during life. On the contrary, in 65 per cent. of all cases there was palpable thickening, though no intimal lesion was found. Indeed, of the instances showing the most marked palpable thickening, excepting the nephritic, no sclerosis could be seen on microscopical study of the vessel wall in 75 per cent. of the cases. Therefore, they conclude, sclerosis of the intima is of minor importance in determining the palpability of a vessel. The authors found sclerosis of the media only rarely, showing that the most marked thickening of the vessel wall may be present independent of an arteriosclerosis. According to the studies of Romberg and of O. Müller, it has been established that very thick-walled arteries are to a certain extent functionally insufficient. But this thickening and impairment of function need not imply an arteriosclerosis. Microscopical examination having shown normal intima and adventitia, the cause of the thickening of the artery, in all cases in which it exists in the absence of arteriosclerosis, must be sought in the media. Thickening of the media plays a certain, though minor, role. It is apparent that the explanation of this palpable thickening must be found principally in a functional change in the media, which



is not demonstrable anatomically. In contradistinction to the arteries in cases of contracted kidneys, these changes are coincident with diminished function, the result being practically the same as that produced by sclerosis of the arteries.

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**The Effect of Cardiac Stasis on the Distribution of Blood to the Internal Organs.**—The general venous stasis of cardiac origin has usually been explained on purely mechanical grounds. No experimental evidence has been brought forward, and proof of other factors is therefore lacking. THACHER (*Deut. Archiv. f. klin. Med.*, 1909, xcvi, 104) has made a careful study of *acute* experimental cardiac insufficiency to determine the probable explanation of the phenomena in man. As he is careful to point out, his work does not apply to *chronic* cardiac insufficiency, which will be considered in a future paper. In rabbits, cats, and dogs, the inflation of a balloon within the right auricle is followed by immediate passive dilatation of the large veins, liver, and brain; but by a fall in the volume curves of the intestine, spleen, kidneys, and extremities. This fall in the volume curve does not coincide with the fall in the arterial pressure that follows such partial obstruction of the right auricle. The blood pressure falls within a few seconds and then remains constant or may recover slightly, whereas the volume curves continue to diminish for as much as five or six minutes longer. The lack of dependence of the volume curves upon the arterial pressure is more striking just after removal of the obstruction, when the blood pressure rises immediately; the volume curves fall temporarily and then recover gradually. In the brain and liver, organs in which vasomotor control is known to be extremely weak, the venous stasis following cardiac obstruction causes an acute passive congestion. In all the other organs examined, decrease in volume was noted, not merely a mechanical result of arterial anæmia, but due to an active contraction of the bloodvessels. The main factor which influences the distribution of blood to the organs is therefore not mechanical, but rather biological, that is, the vasomotor innervation of the organs. The constriction of the vessels in the spleen, kidneys, and extremities is a protective mechanism to prevent the blood pressure from reaching a dangerously low point.

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**The Use of Fats in the Treatment of Disorders of the Stomach.**—As a result of experimental evidence which shows that the liquid fats are devoid of any excitative influence on gastric secretion, and that their presence exerts an inhibitory influence on the normal energy of the secretory process excited by other food-stuffs, a number of observers have administered liquid fats in disturbances of the stomach associated with hyperacidity. The beneficial effects of such treatment are corroborated by the series of cases reported by MOORE and FERGUSON (*Proceed. of the Royal Society of Med.*, 1909, iii, *Med. Sec.*, 25). In sixty-two cases with subjective manifestations of gastric disorder, there were given on consecutive days a plain test-breakfast, and a test breakfast preceded thirty minutes by one ounce of almond oil. In every instance the administration of oil was associated with a marked reduction in both free HCl and total acidity. The greatest reduction was found in those cases, which gave the highest average acidities with the plain

test-breakfast—cases of gastric ulcer, duodenal ulcer, and nervous dyspepsia. In twelve cases with free HCl of 50 or more, the average absolute diminution was twenty. In most instances the absolute diminution of that acidity exceeded that of free HCl. In no cases was the presence of bile-pigments or trypsin noted in the stomach contents after an oil breakfast. In simple forms of hyperacidity the addition of cream and butter in abundance to the diet, with a diminution of the starches, suffice to remove the subjective manifestations. In the more severe almond oil was administered in doses of 1 ounce in the morning, and repeated before subsequent meals if necessary.

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**Veronal in the Treatment of Delirium Tremens.**—MOLLER (*Berl. klin. Woch.*, 1909, xvi, 2340) reports a series of one hundred cases of delirium tremens treated with veronal. There were two deaths, one from double pneumonia, the other in a patient who had had many previous attacks and was extremely weak on admission to the hospital. Aside from these two cases, remarkably good results were obtained. Immediately after admission 1 gram of veronal is given, and if sleep is not produced by this (which is seldom the case), the same dose is repeated after an interval of three hours. As a rule, the patient goes to sleep quickly and remains asleep for six to twelve hours. On waking, he is clear, mentally, and quiet and feels perfectly well. If tremor persists, 0.5 gram of veronal is administered, and in the course of a few hours it disappears. If the patient remains under treatment for a longer time, he is given 0.5 gram of veronal each evening to insure sleep. In rare instances the delirium may not be controlled by the first 2 grams of veronal; an additional gram may then be administered five to six hours later. In one case veronal dermatitis was observed; otherwise no untoward results were noted. The author recommends that the treatment be given an extended trial.

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**Successful Inoculations of Chicken Leukemia.**—HIRSCHFELD and JACOBY (*Ztschr. f. klin. Med.*, 1909, lxi, 107) have repeated the work of Ellermann and Bang on chicken leukemia, and, since these four authors have brought forward the first proof of the transmissibility of leukemia, it is quite possible that their studies may furnish the groundwork for the discovery of the etiology of human leukemia. Their inoculations were made from a leukemic hen furnished by Ellermann and Bang. The results obtained confirm fully those of the last named authors. Of 49 hens inoculated, 18 developed leukemia and 4 pseudo-leukemia. Subcutaneous inoculations of emulsions of liver, spleen, and bone-marrow always gave negative results; the successes followed intravenous injections. The intraperitoneal route was not tried. The disease developed in from one to five months after the inoculation. The blood showed a progressive anemia, with great increase in the total number of leukocytes, mononuclear, non-granular cells predominating. Cell inclusions were at times met with. Leukemic infiltrations of the liver were very extensive, and the bone-marrow presented characteristic changes. The so-called pseudoleukemias were cases in which the typical blood picture was lacking, though the blood-forming organs showed the usual leukemic metaplasia. Unlike Ellermann and Bang,

the authors have been unsuccessful thus far with inoculations of material passed through a Berkefeld filter. Spontaneous cure has been observed in one hen, while Ellermann and Bang had a similar finding in two instances. Cultures from the organs were without result. Attempts to transfer the disease to pigeons, rabbits, and guinea-pigs have failed. The authors believe that each species has its own leukemia, since the human disease has thus far not been successfully transmitted to lower animals.

The authors have begun experiments similar to those detailed above, employing anthropoid apes, inoculated with the blood of myeloid leukemia of man. As yet, no positive results have been obtained, though it is too early to foretell the outcome of the experiments.

Some work has been done with deviation of complement in chicken leukemia, but nothing of value has been determined.

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**Experimental Paroxysmal Tachycardia.**—LEWIS (*Heart*, 1909, i, 98) gives a very complete account of the abnormalities of cardiac rhythm following ligation of the coronaries, and pays especial attention to the production of paroxysms of tachycardia with abrupt onset and cessation. In addition to the production of paroxysmal tachycardia, ligation of the descending branch of the left coronary artery may be the cause of the ventricular extrasystoles, single, successive or retrograde, while ligation of the complete right coronary artery with the subsequent anemia of both auricle and ventricle may cause auricular, "nodal," or ventricular extrasystoles, which may be isolated, frequent, and regularly placed, or in groups. Paroxysms of tachycardia were obtained in nine out of twelve dogs, in which the right coronary artery was tied, but in most instances they only set in an hour or more after the circulation was interfered with. The average ventricular rate during the paroxysms was 253, but in some attacks it was over 400. The rhythm was generally regular, and frequently each ventricular beat was followed by a contraction of the auricle at a time interval which slightly exceeded the *a-v* interval of the normally beating ventricle. The duration of the paroxysms varied from a few seconds to thirty-five minutes. The paroxysms were usually preceded by extrasystoles arising in the ventricle—after a short number of beats, retrogression to the auricle took place. When, however, the original sinus rhythm was rapid, the auricle may remain at its former rate, so that there is a complete auriculoventricular dissociation. In some instances, shortly after the onset of the paroxysm, fibrillation of the auricle occurs, apparently the result of impulses showered upon it from above and below. The fibrillation may terminate in response to sinus or to ventricle. Reversed heart block, showing most of the characteristics of the usual condition, may be met with during the paroxysms. Stimulation of the vagus during the paroxysms of tachycardia usually resulted in dropped auricular beats, without change in the ventricular rhythm, but in three instances complete, temporary standstill of the heart was obtained, followed by a return to the normal rhythm. In some cases, then, the ventricle of the dog is under control of the vagus. Alternation of the ventricles was frequent during the attacks of tachycardia. The paroxysms usually terminated by an abrupt return to the normal rhythm, but sometimes ventricular

fibrillation set in. Irregularities, almost always ventricular extrasystoles, may follow the resumption of normal rhythm. Lewis believes that paroxysmal tachycardia proper, as met with in experiment and in man, is the result of intrinsic change in the heart walls, giving rise to the production of ectopic impulses. The paroxysm has its origin in the ventricular musculature, and is constituted by the establishment of a continuous succession of what are usually designated as extrasystoles. It may be supposed that the paroxysm is the result of a local and enhanced irritability, the offspring of anemia. There is a very close analogy between the experimental tachycardia produced by Lewis and the ventricular form of paroxysmal tachycardia as seen in man.

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**The Effect of Trypsin on Cancer in Mice.**—In order to determine whether trypsin has any actual effect on cancer, RUSHMORE (*Jour. Med. Research*, 1909, xxi, 591) has tested it on mice inoculated with an adenocarcinoma. In those mice in which the tumor was of moderately or very large size the injection of trypsin showed absolutely no beneficial result. In the animals with early tumors cure or spontaneous recovery resulted in 43 per cent., a figure about that which is given as the percentage for spontaneous recovery. Histological examination revealed no evidence of the trypsin having acted on the tumor cells. Those cells around the bloodvessels were in the best condition, and no especial injury to the cells lying on the periphery of the tumor, nearest the point of inoculation, could be made out.

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**The Bacteria of the Stools in Cancer of the Stomach.**—BROWN (*Jour. Amer. Med. Assoc.*, 1909, liii, 1525) has confirmed the findings published from Neusser's clinic as to the presence of Boas-Oppler bacilli in the stools of cases of gastric carcinoma. Smears of the stools are made and stained by Gram's method. A "Gram-negative" stool excludes cancer of the stomach, while a smear showing the presence of the Gram-staining Boas-Oppler bacillus is more easily demonstrated in the stools than in the gastric contents, but it is rather readily confused with other organisms. Brown found Gram-positive stools in all cases of gastric cancer, and Gram-negative stools in both acute and chronic gastric ulcer. In four cases in which the clinical diagnosis was gastric or pyloric ulcer, but in which bacteriological examination showed Gram-positive stools, operation or autopsy revealed a carcinoma.

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**The Causes of Sudden Death.**—BROWN (*Med. Press*, 1909, lxxxvii, 414) has analyzed 183 cases in which death occurred suddenly, before or just after the patient was admitted to the hospital. Liability to sudden death is greatest at two epochs; from birth up to three years, and from thirty years onward. From three to fourteen there is practical immunity, while from fourteen to thirty very few cases occur. Of 63 cases under five years of age, 52 occurred in the first year of life. The postmortem findings show a greater variety in children than in adults. Among the conditions met with were pulmonary collapse, suprarenal hemorrhage, and lymphatism. In more advanced life vascular degeneration is the great cause of sudden death. Of 109 cases over twenty-one years old, heart disease was the cause of death in 31

instances—10 of them being cases of aortic insufficiency. Granular kidney without other cause was found in 18 cases, atheroma of coronary artery in 17, ruptured aneurysm in 14, hemoptysis in phthisis in 9, pneumonia in 8, cerebral hemorrhage in 6, persistent thymus in 1, and in 5 cases no cause for death was found. It was striking that there was an associated granular kidney in 64.2 per cent. of the cases. Of the cardiac conditions, aortic regurgitation and coronary arteriosclerosis were the most frequent findings. When pneumonia was the cause of death, autopsy revealed in every instance gray hepatization—death being apparently due to postcritical syncope.

**The Diagnostic Significance of Hemolysis in Cancer.**—After an attempt to determine the practical clinical value of the hemolytic reactions in cancer and tuberculosis, SMITHIES (*Med. Rec.*, 1909, lxxvi, 901) says that while the blood serum of the majority of patients with malignant disease is capable of destroying normal red blood cells, the same manifestations are possible in non-cancerous subjects. He found the reaction positive in tuberculosis, syphilis, various forms of disease associated with anemia, in infective processes, and in one clinically normal individual. In general, however, while the reaction is positive in the majority of cancerous patients, it is negative in the majority of normal individuals, or of persons suffering from other diseases. In so far, it may have some slight clinical value. While 85 per cent. of one hundred and fifty-three cases of cancer, in all stages, reported by Crile gave a positive hemolytic reaction, Smithies, in a much smaller series of twelve cases, obtained a positive reaction in only 58.3 per cent. In 92 per cent. of fifty-two cases of tuberculosis, Crile reports a reaction of "reverse hemolysis." This was obtained by Smithies in only two out of fifteen instances. The sera from two cases of benign tumor failed to give hemolysis.

**Cardiolysis.**—This operation for the treatment of cardiac insufficiency following on chronic mediastinitis or chronic adherent pericardium was suggested by Brauer, and first performed by Peterson and Simon in 1902. The twenty cases of cardiolysis which have been reported since are reviewed by LECENE (*Archiv. des. mal. du cœur, des vaisseaux, et du sang.*, 1909, ii, 673) who believes that the operation deserves to be used much more frequently. The main indication for cardiolysis is a marked systolic retraction of the precordial region apparently dependent on an adherent pericardium. The most striking results are to be sought (according to Danielson) in those cases in which the signs of cardiac insufficiency fail to clear up under the regular medical treatment. The final outcome depends on the condition of the heart muscle, and for this reason the operation should be performed early and not left as a late resort. In itself the operation is extremely simple and consists in the resection of 8 to 10 cm. of the third, fourth, and fifth ribs and cartilages—thus doing away with the rigid wall against which the heart has been tugging. The time required is about fifteen minutes. No serious results following the operation have been reported. The benefit obtained has varied in the different cases, but in general it has been quite marked, while in several instances confirmed invalids have been enabled to return to work.

## S U R G E R Y.

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UNDER THE CHARGE OF

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**Perforating Ulcer of the Stomach Treated and Cured by Drainage without Suture.**—LEROY and MINET (*Archiv. gen. d. chir.*, 1909, iv, 1101) says that of 53 cases of perforating ulcer of the stomach, operated on by French surgeons, 38 died and 15 recovered. The case here reported had never presented digestive disturbances until five days before the sudden onset of symptoms of perforation. These consisted of slight pain on taking food, and were not relieved until vomiting occurred about a quarter or a half hour afterward. Thirty-six hours after the development of symptoms of perforation, the patient was operated on. On opening the abdomen a considerable quantity of greenish fluid containing numerous particles of food, escaped from the wound and passed to all parts of the abdomen. The chief evidence of trouble was in the region of the stomach and after considerable difficulty an opening was found in the posterior wall near the cardia and lesser curvature. It was about 5 mm. in diameter, had a punched-out appearance and was surrounded by an indurated zone. All efforts to close the opening by suture failed, and the patient's condition becoming bad, further attempts were abandoned. Four drains of large calibre were placed in the abdomen, the first under the liver, the second in the left iliac fossa, the third in Douglas' pouch, and the fourth in the lesser cavity of the peritoneum opposite the gastric perforation. The abdominal wall was then sutured. After a variable course of three months' duration, with much suppuration, the patient finally left the hospital cured.

**Acetone-alcohol for the Disinfection of the Field of Operation.**—HERFF (*Zentralbl. f. Chir.*, 1909, xxvi, 1777) says that acetone-alcohol is the best known disinfecting material for the skin. He disinfects the field of operation in any part as follows: No special previous preparation is made, as by sublimate applications. The part is not washed with soap and water, but the skin is rubbed for five minutes with flannel cloths wet with acetone and alcohol, equal parts. The excess is then sponged away. An alcohol or ether solution of resin was then applied with a brush as a wound protective and the sheets placed in position for the operation. After the operation the wound fluids are wiped dry, and the resin solution is applied to the sutures and the wound. Herff has previously reported concerning the clinical results. He has employed it

in over 280 abdominal sections. There were no severe wound infections. Twice there was slight infection, one from a myoma stump, the other from air infection. The bacteriological and clinical proofs have given to the acetone-alcohol and the wound protective such a high value, and the method is so simple, that it is warmly recommended.

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**Cystitis with Incomplete Retention of Urine.**—CEALIC and STROMINGER (*Ann. d. mal. d. org. gen.-urin.*, 1909, ii, 1787) say that it is well established that inflammation of the bladder without mechanical obstruction, may produce retention of urine, complete or incomplete, the latter more frequently. Three cases of the incomplete type are reported, the cystitis being chronic. In two cases the infection was with gonococci, in the third probably with the colon bacilli. In chronic cystitis the retention is due to the pathological changes in the muscles of the bladder. In the first stage of the disease the muscle is hypertrophied by overwork. In the second stage a sclerous hypertrophy follows, and in the third stage an atrophy. Some of the muscle tissue remains, but is not well coordinated. The fatty tissue is infiltrated among the muscle fibers and disturbs the retraction of the bladder, and this leads to retention. When fluid is injected into the bladder, the desire to urinate becomes intense, while the contractility of the bladder is little accentuated. The urethral sphincter is not involved in the process, so that incontinence does not usually result. There may be incontinence due possibly to an increased sensibility or to a participation of the urethral sphincter, which plays an important part in the act of micturition. Acute retention comes on sometimes in chronic cystitis and is to be explained by attacks of acute cystitis, which produce an inhibitory action upon the bladder muscle.

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**Intrahuman Bone Grafting and Reimplantation of Bone.**—MAC EWEN (*Annals of Surgery*, 1909, i, 959) refers to a case in which the greater part of the humerus was restored by intrahuman transplantation, thirty years ago. The boy who was then operated on is now a man in regular employment, and the details of the case are presented in their entirety. Besides this case three others are mentioned, one illustrating human reimplantation of the flat bones of the skull, and two of restoration by transplantation of human jaw bones. These cases are quoted as examples of many others in which bone grafting and transplantation of bone have been successful. The periosteum plays no part in the bone reproduction after transplantation, and in the majority of the cases the periosteum was not transplanted with the bone. In the case in which the humeral shaft was largely restored thirty years ago, the grafted arm has increased in length, but not proportionately to the increase of the sound one, the latter being now three inches longer. A skiagram shows that the increase in length of the affected arm has taken place almost entirely from the proximal epiphysis. This increase may be taken as an index of the amount of growth, which usually occurs from the proximal humeral epiphysis. All but a minute portion of the distal epiphysis was destroyed by the original osteomyelitis. The grafted portion of tissue, which is easily recognized from the rest of the shaft by its form and contour, has increased markedly in thickness and somewhat in length, so that there has been here interstitial osseous increase.

This indicates that all of the increase in length of the affected shaft did not come from the epiphysis. In another case a large osseous defect in the skull, about two and one-half inches in diameter, was filled in by osseous fragments. The majority of them lived, grew, and threw out ossific matter sufficient to unite them individually to one another and to the rest of the uninjured cranium. Ten years later the skull was firm all over, the bone over the site of prior injury had grown in proportion to the rest of the skull. In a third case, the transverse ramus of the jaw, removed years before, was restored by transplantation of a piece of rib, of proper length to fill the gap. The rib was removed subperiosteally, and divided longitudinally into strips. These were inserted into the gap in the soft tissues, and secured to the ends of the bone on either side, so as to keep the right mandible in its proper position. The operation was done through an external incision below the jaw and the wound was closed over the transplanted bone and dressed. One small portion of bone was later shed. Six years after the operation the transplanted bone had thickened. The patient is now perfectly well, and can use the mouth freely for mastication; she speaks well, and the face is symmetrical.

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**Ligation of the Thyroid Vessels in Certain Cases of Hyperthyroidism.**—MAYO (*Annals of Surgery*, 1909, 1, 1018) says that the operation is indicated in those suffering from mild symptoms of hyperthyroidism, and those in whom the diagnosis is made early, possibly before the less important eye symptoms or even goitre is present. In cases, which are hardly severe enough to warrant a thyroidectomy, the ligation of the vessels will often produce a cure in a few weeks, with but little risk of special medication. It is indicated in that larger group of acute severe exophthalmic goitres, and in the chronic and very sick patients, who, having exhausted all forms of treatment, are now suffering with various secondary symptoms, dilatations and degeneration of the heart, fat liver, soft spleen, diseased kidneys, which have resulted from the toxins, as seen in the latter stage of Grave's disease, changes which are after all the final cause of death. All severe cases should be under observation for a short time at least and some cases for a considerable time, to improve their condition if possible, even before a ligation. 580 cases have been operated on at St. Mary's Hospital. Of these 225 were by ligation of the superior thyroid arteries and veins, 138 were ligated sufficiently long ago to make their report of value. There was slight improvement in 9 cases, great improvement in 44 cases, very marked improvement in 11 cases, 4 cases are absolutely well, and in 9 cases of questionable exophthalmic goitre, there was no improvement. In the majority of cases the ligation is made as a definite step in a graduated operation to reduce excessive secretion of the gland, and some of the cases are yet to be operated on for the removal of part of the gland as a secondary procedure.

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**Musculospiral Paralysis Complicating Fracture of the Humerus.**—SCUDDER (*Annals of Surgery*, 1909, 1, 1118) says that musculospiral paralysis occurs in from 4 to 8 per cent. of cases of fracture of the humerus. Fracture of the middle of the humerus is most frequently



complicated by musculospiral paralysis. It may occur at any age from fracture of the humerus. It is primary if it dates from the accident and it is secondary if it is subsequent to the accident. Primary paralysis indicates a more severe injury to the nerve than does secondary paralysis. The diagnosis of the exact pathological condition of the nerve following trauma to it, is of the greatest importance and is difficult to determine. Progressive impairment of function or stationary paralysis of the nerve, complicating fracture of the humerus justifies and may demand operation. Operation means the release of the nerve from compression or tension and often resection and suture, and always guarding against recurrent compression or stretching. A late suture (months after the injury), is attended by technical difficulties not present in an early suture (soon after the injury). Resection of the humerus to allow of approximation of the divided ends of the musculospiral nerve is a good procedure (Allis, Philadelphia), but not until nerve suture *à distance* has first been carefully employed. Electrical reactions cannot determine the pathological condition. They are of value in determining the course of events. The prognosis after operation is good; the earlier a necessary operation is done the speedier the cure. Exercise of paralyzed muscles by electric stimulation (galvanism) is helpful. Sensory symptoms are variable; in general the sensory symptoms have no relation to the degree of motor loss.

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**Non-operative Reduction in the Treatment of Traumatic Coxa Vara and Valga.**—SPRENGEL (*Zentralb. f. Chir.*, 1909, xxxvi, 1745) takes up especially the treatment of these conditions, the anatomical and clinical aspects having been discussed in previous papers on the subject. Almost without exception it begins with a trauma, which results in an epiphyseal separation of the femoral head. The obvious treatment, therefore, is to replace the separated surfaces in position. A case is reported in which the traumatic coxa vara came to treatment three days after the accident. The displacement was so slight that the real and functional shortening was only 1 cm. The external rotation, limitation of movement, age (seventeen years), the preceding injury, and the x-rays made the diagnosis positive. The replacement was effected in narcosis, by forcible extreme abduction, and as far as possible internal rotation with fixation in this position by plaster-of-Paris. This position was maintained with several changes of the plaster dressing until it reached only to the knee, for four months. The result was very satisfactory. The shortening and external rotation had disappeared. Abduction and internal rotation were slightly limited and there was little disturbance of the gait. A somewhat similar case of traumatic coxa valga is also reported. A thirteen-year-old student, six weeks before admission, had stepped in a hole, and was immediately seized with a severe pain in the right hip. There was associated external rotation and a marked disturbance of the gait. Three weeks before the accident, however, there was present a slight pain in the same hip. On admission, the right femur was markedly rotated externally, slightly abducted, and somewhat flexed. There was no functional shortening, but a real shortening of 2 cm. which was overcome by a sinking of the pelvis. The x-rays showed a separation of the epiphysis, with a displacement in the position

of coxa valga. Reduction was performed in narcosis with forcible adduction and internal rotation. The correction was successful only when the internal rotation was carried out. It could be easily fixed in adduction and in internal rotation, which position was maintained for two months, when the treatment was changed to medical and mechanical methods. About a month later the function in both limbs was about the same. There was real shortening of 1 cm., which was overcome by sinking of the pelvis on that side. The external rotation was hardly recognizable, flexion could be made to only about one-half of the normal, rotation was the same as on the left side, and abduction to about 20 to 25 degrees was possible. There was a slight dragging of the right leg in walking. Sprengel emphasizes the importance of the use of forcible correction of the deformity as well as the prolonged immobilization afterward. Consolidation here takes place slowly, and the obliquity of the neck favors displacement of the bone ends. A correct diagnosis of the coxa vara or valga is also of great importance. He has seen about 20 cases in most of which the diagnosis of coxitis had been made.

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**Double Traumatic Dislocation of the Shoulder.**—LINDEMANN (*Deut. Ztschr. f. Chir.*, 1909, cii, 561) saw in three months, three cases of simultaneous, traumatic dislocation of the two shoulders. He saw also two cases of simultaneous dislocation of both shoulders in persons who had previously suffered from a dislocation of one or the other shoulder; and in which there occurred a dislocation in the left shoulder, previously sound. In children dislocations of the shoulder are rare, in middle age they are not common, and only in old age are they relatively common. Only one of Lindemann's patients was young (eighteen years). The others were thirty-six, forty-seven, fifty-seven, sixty, and sixty-six years of age. It is believed that changes in the joint and ligaments and overlying soft tissues play an important role, as when they are atrophied. In the young and middle aged these structures are so strong that the bones are more frequently fractured than dislocated. The relaxation of the ligaments and other soft structures coming on with age, gradually loosens the joint. Degenerative changes also play a part, and these come on in some cases earlier than in others, especially in the working classes, among whom the dislocations most frequently occur. Severe violence is not always necessary, even for a double dislocation. They may be due to direct or indirect violence or to muscular contraction. All the dislocations observed by Lindemann were preglenoidal, three of them purely subcoracoid, in which the x-rays showed no changes in the bones. In one case there was a shadow, probably from a broken-off piece of bone. A tearing off of the greater tuberosity was shown in one of the cases, and on the same side a fracture of the glenoid margin. In three recent cases reduction by Kocher's method was easy, without narcosis, but with small doses of morphine. In only one of the recent cases was narcosis necessary. In one case in which the dislocation was three months old, the reduction was unsuccessful in the first attempt, and successful on the second attempt under narcosis. On the other side, in the same case, the careful efforts at reduction on account of the evident atrophy, led to a fracture of the shaft of the humerus at the deltoid

insertion. In one case there soon developed recurrent dislocations in one shoulder and later in the other. In this case altogether about two hundred dislocations occurred, and in one day as many as three. In the past four years the patient has been unable to work.

**Volvulus of the Intestines as a Disease of Hungry Men.**—SPASOKUKOZKY (*Archiv. f. klin. Chir.*, 1909, xclx, 211) says that he has collected observations for eleven years, in the government hospital at Smolensk. About 70 per cent. of the patients are peasants, and nearly all of them country people. This fact is of especial importance since the literature of ileus concerns itself chiefly with patients from the large cities. It is generally considered that volvulus of the sigmoid flexure is the most common, while other parts of the intestinal tract are very rarely involved. Lindemann's observations lead to a different conclusion. Of the 96 cases of acute intestinal obstruction, there were 8 of invagination, 8 of tumor (cancer, tuberculosis), 5 of properitoneal hernia, 20 of strangulated hernia, 8 of unknown cause, and 47 of intestinal volvulus. Of the 47 cases of volvulus, 18 were of the sigmoid flexure, 1 of the cecum, and 28 of the small intestine. Concerning the question of the turning of the intestine, there are three chief factors: (1) The intestinal peristalsis which is permanent and is increased by the taking of food and the work of the intestine. (2) The intestinal contents; moderate filling of the intestine occurs with a meat diet, and excessive filling with a vegetable diet. At times the intestines are absolutely empty. Two cases were observed in which the total contents of the small intestines could be held in the hollow of the two hands. (3) Abdominal pressure; this varies between extreme limits, as between the lax abdominal wall of the multipara, and the tense abdominal wall of a strong man. In one patient who was extremely emaciated the operation showed that all the small intestines lay to the left of the sigmoid flexure, which was snared by them and was very much dilated. In considering the mechanism of this case and an analogous one, Spasokukozky is convinced that there must have been a time when the small pelvis was free of small intestines and filled by the sigmoid flexure. The small intestines, empty because of hunger, moved upward. The vomiting caused further movement upward into the left hypochondrium. By the taking of nourishment or by a change in position, the sigmoid moved out of the pelvis. The small intestines then took its place, passing over and constricting the two ends of the sigmoid.

## THERAPEUTICS.

UNDER THE CHARGE OF

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**The Hemoptysis of Phthisis and its Treatment.**—REICHE (*Zeit. f. aerzt. Fortbildung*, 1909, xv, 465) says that the patient should be kept

in bed and avoid all physical and mental effort. Warm drinks, alcohol, and effervescent drinks should be prohibited. The food and drink of the patient should be reduced to a minimum. An ice bag on the chest corresponding to the part of the lung involved may be of service. Morphine should be prescribed to stop the cough. Reiche says that digitalis acts well in some cases, those in which the bleeding is dependent upon a congestion of the venous pulmonary system. If the arterial system is the source of hemorrhage, digitalis is unsafe. Reiche admits that the differential diagnosis of these two forms of pulmonary hemorrhage is difficult and often impossible. He believes that adrenalin is harmful and that ergot has little or no effect in pulmonary hemorrhage. He has used gelatin with no convincing results of its efficacy. The ingestion of gelatin by the mouth probably has little or no effect upon pulmonary hemorrhage. While the subcutaneous injection is painful, Reiche has seen good results with the use of calcium chloride in hemoptysis in some cases. He recommends a dose of 4 grams during the twenty-four hours, divided into two doses. The use of calcium chloride is perfectly safe, but its effect varies considerably in individual cases. Furthermore, it is always difficult to estimate a definite therapeutic effect of a drug in pulmonary hemorrhage which often ceases spontaneously.

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**The Treatment of Severe Anemias with Human Blood Transfusion.**—WEBER (*Deut. Archiv f. klin. Med.*, 1909, i, ii, 165) reports seven cases of severe primary anemia which he treated by human blood transfusion. He obtained about 25 c.c. of blood by aspirating the median basilic vein of a healthy young man. This blood was stirred for ten minutes with a sterile glass rod in a sterile vessel and then filtered. He used this defibrinated blood as a stock solution. The maximum dose of this solution was 5 c.c. He injected this solution by means of a syringe into the median basilic vein of the patient. All of the cases received at least three transfusions during a period of six weeks or more, and they all improved. The percentage of hemoglobin and the number of red blood cells increased and at the same time the symptoms improved. Untoward effects after the transfusion were frequent; but of short duration and not serious. The most common untoward effects were moderate fever, headache, ringing in the ears, malaise, and dyspnoea. In one case transfusion was followed by fever lasting four days, with a small area of consolidation in the right lung, probably due to infarction. Weber ascribes the beneficial effects of blood transfusions to a stimulation of the blood-making cells of the bone marrow. He observed always after the injections a great increase in the number of nucleated red blood cells. Therefore, he advocates the use of only 5 c.c. of blood at each transfusion, since the beneficial effects are not due to an increase in the volume of the blood. Weber claims that his method is simple and safe, with equal or better results than with arsenic or the larger transfusions.

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**Camphor and Pneumococci.**—SEIBERT (*Münch. med. Woch.*, 1909, xxxvi, 1834) treated a series of 21 cases of pneumonia with injections of camphor oil. The age of the youngest patient was four years, and

the oldest seventy-two years. He does not give detailed reports of his cases, nor does he state the average duration of the disease under this treatment. The camphor was administered in the form of a 20 per cent. solution in oil. He gave it in variable doses as high as 12 c.c. at a single dose. He repeated the dose every twelve hours until the pulse, respirations, and temperature became normal, and then every twenty-four hours until the lungs were clear. Seibert noted that no crisis occurred in any case, but that a gradual improvement followed immediately after the first injection and continued to recovery in every case. He also adds that the duration of the disease was considerably shortened. Seibert thinks that the effect of camphor may be explained by a direct bactericidal action upon the pneumococci, in addition to the stimulating action of the camphor. The number of Seibert's cases does not allow one to draw any definite conclusions, and furthermore, his series of cases occurred during the summer months when pneumonia is, as a rule, less virulent.

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**A New Method of Treatment of Epilepsy.**—BRATZ and SCHLOCKOW (*Deut. med. Woch.*, 1909, xxvii, 1184) write concerning the treatment of epilepsy in the state institute for epileptics at Wuhlgarten. They treated 50 cases of epilepsy with sabromin. Sabromin is similar in structure to sajodin, being the calcium salt of dibrombehndie acid. It contains 29 per cent. of bromine; 3 grams of sabromin seems to equal 4 to 6 grams of potassium bromide in strength. They gave the sabromin in tablet form, each tablet containing 0.5 gram. It was found better to give the remedy one hour after meals. It was especially noteworthy to see the disappearance of various skin eruptions, which had been caused by other bromine preparations. Furthermore, no case of skin eruption was observed during the use of sabromin. This has been explained by the fact that less bromine is furnished to the body by sabromin. However, it seems to be a fact that sabromin, although it contains less bromine, is able to exercise the same anti-epileptic action as the other bromine salts. They state that 4 grams of sabromin contains about one-half the amount of bromine in an equal quantity of potassium bromide, though it equals 6 grams of potassium bromide in efficacy. To explain its action it has been suggested that sabromin combines directly with the nervous tissue.

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**A New Bromine Preparation in the Treatment of Epilepsy.**—HAYMANN (*Med. Klin.*, 1908, l, 1910) gives the results obtained in the psychiatric clinic at Freiburg with the use of sabromin in the treatment of epilepsy. Some of the patients have been under the treatment for seven months, and many for from two to four months. Haymann found that the remedy was well borne, causing no untoward symptoms on the part of the gastro-intestinal tract. The patients took the remedy with ease, it being odorless and almost tasteless. No bromine acne was observed during the use of sabromin; on the other hand, already existing skin eruptions cleared up. Two tablets of 0.5 gram each, given three times a day, gave the necessary saturation of the body with bromine. This same effect, he says, would not be obtained with 4 grams of potassium

bromide. Haymann determined that the dose could be considerably increased without the danger of poisonous symptoms. It appears plausible from the chemical structure of sabromin that its action is slow, and at the same time prolonged. Haymann says that his clinical observations agree with this theory. No patient became accustomed to the remedy, so that it was not necessary to increase the dosage.

**The Action of Fats in Excessive Gastric Secretion.**—MARTINET (*Presse méd.*, 1909, lviii, 515) advocates the use of olive oil in cases of excessive gastric secretion, such as ulcer of the stomach, simple hyperchlorhydria, and gastrosuecorrhœa. He also believes that from 100 to 150 grams of olive oil taken before breakfast is beneficial in the treatment of gallstones. Often the olive oil is objectionable, and then the fat may be prescribed in the form of fresh milk or cream. Fresh almonds up to an amount of 80 to 100 grams a day may also be used to furnish the required amount of fat. Fresh bone marrow spread on bread in place of butter is another method suggested for supplying the fat. He also suggests that olive oil may be substituted for butter in the preparation of food, since it is more easily digestible than other fats. Olive oil, he claims, diminishes gastric secretion, regulates the bowels, and supplies easily digestible nutriment.

**The Treatment of Gastric Ulcer with Iron Chloride Gelatin.**—BOURGET (*Therap. Monats.*, 1909, vii, 353) has used, for a number of years, stomach lavage with a 1 per cent. solution of iron chloride for the treatment of gastric ulcer. He replies to the objections of some against the use of the stomach tube in ulcer of the stomach that he has used it thousands of times with no bad results. On the contrary, most of his cases have been cured in fourteen days, and some even in still less time. Since, in practice, it is often inconvenient to use a stomach tube, he has endeavored to apply a modification of this treatment by giving the iron chloride in gelatin. He prepares this in the following manner: 100 grams of gelatin is dissolved in 100 grams of water and 100 grams of glycerin. To this he adds 50 grams of a 10 per cent. solution of iron chloride. The addition of the iron chloride forms a precipitate. The mixture is stirred vigorously while warm in order to secure a homogeneous distribution of this precipitate. The mixture is then poured into the moulds of 1 c.c. capacity and allowed to harden. Two or three of these tablets are given two or three hours after meals. Bourget follows this routine: 8 A.M., milk and zwiebach; 10 A.M., one tablet; 10.30 A.M., 100 to 150 grams of alkaline water; 12 noon, milk and rice; 3 P.M., one tablet; 3.30 P.M. to 4, 150 grams of alkaline water; 6 P.M., milk and rice; 9 P.M., one tablet; 10 P.M., 150 grams alkaline water. The prescription for the alkaline water is as follows:

R—Natrii bicarb. puriss.	. . . . .	8.0
Natrii phosph. sicci.	. . . . .	4.0
Natrii sulph. sicci.	. . . . .	2.0

The prescription is to be divided into powders.

Dissolve one of these powders in 1 liter of cold water.

The effect of this method of treatment is very favorable, especially

upon the pain. In the severe cases with bleeding he begins the treatment by lavage with a 1 per cent. iron chloride solution and then follows with the iron chloride gelatin. In all the cases so treated the bleeding stopped immediately and did not recur. Bourget adds that the iron chloride gelatin has the further advantage of combating the anemia.

**The Treatment of Stokes-Adams Syndrome.**—WILCOX (*Boston Med. and Surg. Jour.*, 1909, xxv, 825) recommends in the treatment of Stokes-Adams syndrome the use of atropine to diminish the irritability of the pneumogastric terminals, and strychnine to increase the force and frequency of the ventricular systole. He adds that atropine is useless when the symptoms are dependent upon a myocarditis. Alcohol in some cases has seemed to diminish the attacks. Wilcox also secured good results by the use of cactus grandiflorus given in the form of the fluid extract in doses of 30 drops. After the acute attack has subsided he gives iodide of arsenic in doses of 1 mg. three times a day. Since the presence of gummas in the bundle of His has been determined in a number of autopsies, he thinks it wise to try mercurial inunctions or intramuscular injections of iodide of mercury in oil. At the same time strontium iodide should be given in increasing doses.

## PEDIATRICS.

UNDER THE CHARGE OF

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**The Effect of Cathartic Drugs in Children.**—I. A. ABT (*Archives Pediatrics*, 1909, xxvi, 836) reports the result of observations made to determine the therapeutic limitations of cathartic drugs in children. Calomel, castor-oil, and Epsom salts were given 125 times to 22 children. The stools were examined before administration began and also twenty-four hours afterward, particular stress being laid on the presence of blood and mucus in the feces; these elements being taken as an index of the degree of irritation produced. Calomel in 1-grain doses, and the same amount in divided doses, showed on the following day mucus, and occasionally blood in the stools. Two or 3 grains given at one dose showed both blood and mucus, which continued for two and three days. When calomel was given in daily divided doses ( $\frac{1}{10}$  grain) for a consecutive number of days, the reaction for mucus and blood increased in intensity from day to day.

Magnesium sulphate in single doses of 1 dram of a saturated solution resulted in slight irritation, but no blood. Larger doses, 1 dram for three successive days, showed the reaction for blood and considerable mucus, though not as much as followed repeated doses of calomel. Castor oil in single doses of 1 dram showed no irritation. Two drams at one dose administered to older children showed irritation in one case

and none in the other. One dram of the oil for three successive nights caused the reaction of irritation after the third dose. A study of the results shows that all three cathartics are capable of producing signs of irritation if the dose is large enough or continued for a period of time. Calomel seems to give the greatest irritation with average doses, in the shortest time. Castor-oil gives the least reaction. The Weber and benzdene tests were employed to demonstrate the presence of blood. It was observed that green stools were especially frequent after calomel and that the odor was more offensive. Calomel also produced the most marked effect on oxidized bile pigment, when present. The quantity of unoxidized bile pigment was usually larger after catharsis.

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**Flexner and Jobling's Anti-serum in Cerebrospinal Meningitis.**—PERCY MARSH and OWEN WILLIAMS (*Brit. Jour. Children's Dis.*, 1909, vi, 299) report the results of Flexner and Jobling's antiserum in 18 consecutive cases of cerebrospinal meningitis in children. The examination of cerebrospinal fluid from lumbar puncture is essential in every case of meningitis. Besides the tuberculous, the most common form was found to be due to *Diplococcus meningitidis*, a Gram-negative organism. For this form the antiserum is most serviceable. Flexner's statistics show a reduction of mortality in all forms of the disease of 29.6 per cent. In 523 cases tested with the serum 368 recovered. The efficacy of the serum is increased the earlier it is given. In Flexner's tables of children under two years, of eleven treated in the first three days one died; of eleven treated before the seventh day four died; whereas of 29 treated after seven days 20 died. Of the 18 cases reported by Marsh and Williams the first four were tuberculous meningitis, in which *Diplococcus meningitidis* was also isolated, showing that the latter may occur merely as a secondary infection to other forms. In the remaining 14 cases the diplococcus alone was isolated in every instance. Twelve of the 14 were under one year. There were 7 recoveries in the series, 5 of which were under one year. Only 3 cases were obtained in the first few days of illness and all of these recovered, two being infants of three and five months, respectively. In the other case the serum was injected from the seventh day to as late as the fifty-eighth day. In all the cases the fluid from the first puncture showed turbidity. It contained albumin in increased quantity, reduced Fehling's solution only slightly, and contained polymorphonuclear leukocytes, vacuolated cells, and the diplococcus both intra- and extra-cellular. After the first and second injection of serum the number of organisms is decidedly reduced, and after the seventh day this fluid becomes clear and free from organisms. The dosage depends on the age of the patient, the severity of the infection and the number of organisms present. Dunn, of Boston, advocates in older children and adults four doses of 30 c.c. each, on successive days. Smaller doses, less frequently repeated, gave better results. In the present series a child of four received an initial dose of 25 c.c., which was repeated every fourth day up to a total of 130 c.c. A child of three months received, but one injection of 10 c.c. Another of five months received one of 10 c.c. and later one of 7 c.c. These cases are among the recoveries. When purulent exudate had formed on the brain and cord before the serum was injected, the results were



less favorable, as the serum is bactericidal and only slightly antitoxic. On this account it is injected directly into the spinal canal. In lumbar puncture one should use a needle accurately fitting a syringe holding 15 c.c. If the fluid shows turbidity remove 30 to 40 c.c. of it, warm the anti-serum to body temperature, and inject slowly after removing the fluid. Every turbid specimen of fluid premises the diplococcus. In none of the recovered cases so far treated is there any evidence of hydrocephalus, mental impairment, or other disabilities usually following this disease.

**The Urine in Gastro-intestinal Diseases of Infancy.**—JOHN LOVETT MORSE and BRONSON CROTHERS (*Archives of Pediatrics*, August, 1909, xxvi, 561) quote the opinion of Koplik, who believes that renal complication is quite a factor in gastro-enteritis, and that often the stupor, delirium, convulsions, and œdema in severe cases are due to uremia. Hohlfeld, in a number of investigations, found that in the majority of fatal gastro-enteric cases the urine contained albumin and a few casts. In 35 autopsies the changes in the kidneys were found to be parenchymatous. He believes that toxemia and kidney irritation react on each other and offer a bad prognosis. Chapin, in 86 cases, records 75 as having albumin and casts in the urine; also the majority of the fatal cases had albumin in the urine. The authors tested the urine in 300 babies suffering from gastro-intestinal conditions. The examinations were consecutive. The tests for albumin were nitric acid (cold), acetic acid and heat, or both. In children with chronic digestive disturbances albumin was found in but 8 per cent. There was usually only a trace of it, with no casts and no œdema. The presence of the albumin had no effect on the prognosis. In acute conditions albumin was found in a little over 10 per cent. of the cases. There was usually only a trace of it without casts or blood and this had no effect on prognosis. The mortality was considerably higher in the intestinal cases with albumin than without it. These were not accompanied by œdema. The authors conclude that the pathological condition in the kidneys does not progress beyond cloudy swelling or acute hyperemia. There was nothing to suggest any causative relation between the affection of the kidneys and stupor, restlessness, and convulsion. These they believe are due to toxemia and not to uremia. The large number of cases examined give a general idea of the frequency of renal complication, and the importance of the urinary findings in prognosis from the clinical side. No autopsies were reported.

## OBSTETRICS.

UNDER THE CHARGE OF

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**The Factors Producing Internal Rotation in Labor.**—PARAMORE (*Jour. Obstet. and Gyn. Brit. Empire*, October, 1909) has reviewed the literature of the subject and concludes from this and from his own investiga-

tions that descent and internal rotation take place essentially as follows: When flexion is good the point of impact of the vertex occurs at the extremity of a line drawn at right angles from the centre of the plane of the brim, reaching the pelvic floor in the region of the coccyx. The muscular fibers arising from the spines of the ischia and inserted into the coccyx, and the muscular fibers extending from the anus to the coccyx are hypertrophied during pregnancy. They form distinct muscular bundles very tender on pressure and capable of contraction. The vertex first impinges against this portion of the pelvic floor and uterine contractions force the pelvic floor downward at this point. The pelvic floor yields to the centre, the coccyx slopes downward and forward, forming an inclined plane down which the vertex is pressed. With the forehead posterior it descends behind the vertex, occupying the middle line posteriorly. The transverse diameters of the pelvis become diminished, while the anteroposterior are increased as the outlet is reached. The forehead is forced toward the hollow of the sacrum by the increased pressure between it and the posterolateral surfaces of the pelvic wall. If the forehead be anterior, cases may be divided into groups, one in which the head is well flexed, and one in which the head is not well flexed. When flexion is good the vertex meets the pelvic floor in the region of the coccyx, and is gradually forced lower and yet anterior toward the symphysis. As labor continues the forehead is compressed obliquely upward. The descent of the forehead is prevented by the projecting forward of the vertex, the pressure of the pelvic floor preventing the vertex and occiput from retreating. The foetal chest forced against the chin prevents the forehead from ascending above the pelvic brim; the forehead passes into the larger transverse diameter, allowing the cranial axial line to move toward the symphysis. Uterine contractions and the frictional resistance of the side wall of the pelvis and forehead cause the occiput gradually to rotate to the front, while the forehead turns into the hollow of the sacrum. The factors concerned in causing rotation are the expulsive force from above, the obstructing central fixing force from below, the shape of the pelvis, and the shape, size, consistence, and position of the foetal head

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**Polyhydramnios Complicated with Œdema.**—CAIE (*Jour. Obst. and Gyn. Brit. Empire*, October, 1909) reports the case of a patient in her second pregnancy, who, at the sixth month, was taken with severe pain in the back and side with general abdominal distress. On examination there was marked œdema of the lower extremities, dyspnœa and irregular heart action, with loud mitral and pulmonary bruits. The pain was referred to the left side about the lower dorsal vertebrae, extending to the umbilicus. The abdomen was tense and dull, and foetal heart sounds could not be heard. The urine was scanty, containing a trace of albumin, and on vaginal examination nothing could be detected except ballottement which was very plainly present. Under rest and medical treatment the patient's condition somewhat improved. A month later the patient was very much worse. Œdema had become so pronounced that the patient was confined to her bed. Emaciation had developed and the facial expression resembled that of ovarian cyst.

The heart sounds were irregular and intermittent. On attempting to induce labor the œdema of the vulva was so pronounced that this procedure was impossible. Small trocars were inserted in the labia, and when the œdema had sufficiently subsided the membranes were ruptured. Labor gradually developed and the patient was delivered by forceps of a dead child. The puerperal period was complicated by intense after-pain, with temperature rising to  $100^{\circ}$  several times. Over the abdomen and inner sides of the thighs urticaria of a very persistent and irritable type developed. On the eighth day the patient had a chill with temperature rising to  $104^{\circ}$ . This speedily subsided, the patient ultimately making a good recovery. The amniotic liquid was analyzed and found alkaline, with a specific gravity of 1010, and contained urea and albumin with epithelial scales and various salts.

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**Pregnancy Complicated by Nephrectomy and Ovariectomy.**—ANDREWS (*Jour. Obst. and Gyn. Brit. Empire*, October, 1909) reports the case of a small, delicate-looking woman, aged thirty-two years, who had had the right kidney removed for hydronephrosis. The kidney had been movable and the surgeon who operated did not intend to remove it; but on exploration it bled so freely and was so disorganized that removal became imperative. When Andrews saw this patient she was seven months pregnant, and in addition had a cystic tumor the size of a foetal head on the right side of the abdomen. She was admitted to the hospital and upon operation a unilocular cyst containing three pints of fluid was removed. The patient had severe vomiting after operation with rapid pulse, and seventy-two hours after the removal of the tumor a male child was spontaneously born. Mother and child made a good recovery. The patient subsequently had her tenth child within a year of the ovariectomy. This patient's case demonstrates the possibility of successful pregnancy after the removal of one kidney, even though the patient's condition was complicated by ovarian tumor.

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**Complete Rupture of the Uterus Treated by Operation.**—LEA (*Jour. Obst. and Gyn. Brit. Empire*, October, 1909) reports 5 cases of rupture of the uterus treated by abdominal hysterectomy, with 3 recoveries, at St. Mary's Hospital, Manchester, within the last three years. His own case was that of a woman in her third labor, the two previous having been terminated by forceps. The membranes ruptured before the head descended and engaged, when the physician called to see the patient, applied the forceps, making repeated efforts to deliver under anesthesia, without success. Shortly afterward the patient had marked pallor and rapid pulse with slight hemorrhage from the vagina. She was immediately transferred to the hospital. On admission, the foetal head was lying above the pelvic brim, and evidently the uterus had completely ruptured. On section a full-term foetus was found among the intestines, the head resting upon the promontory of the sacrum. The placenta had also been expelled. The anterior wall of the uterus had been completely torn across, the tear extending into the left broad ligament. The uterus was rapidly removed by clamping the upper portions of the broad ligament, the cervix, which was widely dilated and torn, was inverted toward the vagina, and the peritoneum was stitched over

the stump. The abdomen was closed without drainage. The vagina was thoroughly cleansed, and gauze packing introduced within the cervix. Intravenous saline transfusion was given. The patient made an almost uncomplicated recovery. On examination the pelvis was found considerably contracted in the anteroposterior diameter. This case calls attention to the familiar error of applying forceps to the foetal head before engagement and descent.

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**Suprasymphyseal Section for Pelvis of Moderate Contraction.**—KUPFERBERG (*Zentralbl. f. Gyn.*, No. 45, 1909) reports 4 successful suprasymphyseal sections with recoveries of both mothers and children. He had previously performed 10 pubiotomies, 6 of them followed by operative delivery, and 4 by spontaneous expulsion of the child. In one case after pubiotomy and the high application of the forceps, it was necessary to perforate the child to secure delivery. In one case after pubiotomy, when the operator waited for spontaneous delivery, fever developed and he was obliged to terminate labor by the Porro operation. In one case after pubiotomy severe expulsive efforts developed and the child perished during the stage of expulsion. The result, so far as the mother was concerned, was 100 per cent. recoveries, and for the children 80 per cent. recoveries. The puerperal period was, however, complicated by lacerations and by the formation of hematoma. The shortest time taken for recovery was fourteen days, and the longest five weeks. In his ten patients recovery seemed excellent, the patients retaining the power of motion without complication.

In choosing the suprasymphyseal section he employed Latzko's method. This consists in making a transverse incision through the fascia and abdominal wall above the pubes and a longitudinal incision through the lower uterine segment and cervix. The bladder is partially filled by salt solution and the peritoneal tissue is separated from the connective tissue in the vicinity of the bladder by gauze pressure. One of the four cases was of especial interest. The patient had a contracted pelvis, the true conjugate measuring 8.5 cm. An effort was made during labor to deliver the patient with the forceps, but the blades slipped from the head. Hematoma developed in the left wall of the vagina and rapidly increased in size. On admission it was almost impossible to examine the patient because the hematoma nearly filled the vagina. A suprasymphyseal section was then performed with great difficulty, because the patient was very fat. The child was delivered by forceps with very free bleeding. It weighed seven and three-quarter pounds and was delivered alive. The peritoneum was lacerated to some extent during labor and immediately repaired. The bladder was punctured by a needle during the operation, and a stitch was taken over the point of puncture, and permanent drainage by a catheter instituted. Thirty-six hours after operation symptoms of peritonitis developed, and the abdomen was opened on the left side, under local anesthesia. The peritoneum was drained and an artificial anus made in the iliac region. As the patient did not improve in twenty-four hours, incision was practised on the right side of the abdomen, when an ovarian cyst the size of a child's head, with twisted pedicle, was discovered. This was removed and the peritoneal cavity drained.

The patient commenced speedily to improve and was convalescent in fifteen weeks. On examination before her discharge the uterus was normal in size, drawn a little toward the right side, the cervical portion slightly fixed. Both intestinal fistulas had closed and the patient's condition was satisfactory.

In the Clinic in Mainz the following is the treatment of medium grades of contracted pelvis: Under favorable conditions, with examination under anesthesia from the thirty-second to the thirty-fourth week, the induction of labor. If the patient comes to full term and goes into labor and the child dies, embryotomy. If the child is living and in good condition, examination is made under anesthesia, and if engagement and descent are impossible and the patient is a primipara, suprasymphyseal section is performed. If the patient is a multipara, pubiotomy is selected.

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## GYNECOLOGY.

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UNDER THE CHARGE OF

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**The Prevention of Adhesions in Abdominal Surgery.**—J. C. WEBSTER (*Surg., Gyn., and Obst.*, 1909, viii, 574) states that such general conditions as prolonged anesthesia, systemic weakness, and anemia may contribute to the formation of adhesions following abdominal operations. But, experimentally, in dogs such adhesions may be produced by undue exposure to dry air, cold air, mechanical trauma, and cultures of micro-organisms. Webster thinks we should, therefore, avoid these factors as far as possible in abdominal surgery. The temperature of the operating room should be as high as 90° F., the degree of humidity high, the peritoneum covered as much as possible with gauze wet in hot salt solution, self-retaining, if any, retractors used, a minimum amount of sponging done, and, so far as possible, all denuded areas covered either by surrounding peritoneum sutured with fine catgut, or by omental grafts.

**Results of the Treatment of Uterine Carcinoma.**—G. KLEIN (*Monatschrift f. Geburtsh. u. Gynäk.*, 1909, xxix, 710) found among 15,074 patients of his private practice and the Polyelinie of the Munich University, 421, or 2.79 per cent., with carcinoma of the uterus; 106 of these refused radical operation. Of the remaining 315, only 126 were radically operated upon, giving an operability of 40 per cent., which compares favorably with the findings of other operators. The primary mortality was greater in abdominal radical operation than in vaginal operation—in private practice 16.1 per cent., in the Polyelinie, 9.5 per cent. mortality. Among 204 cases whose histories were obtainable after five years it was found that only 8, or 3.6 per cent., were absolutely cured. Klein severely

criticises the methods of "decorative juggling" of statistics, and adds that recourse to such measures would most favorably affect the results obtained, but would obscure real facts. Careful study of reported statistics would reveal about the percentage of cures obtained in this instance. The operative prognosis in uterine cancer at best is very unfavorable.

**Fibromas of the Uterus.**—ELLICE McDONALD (*Jour. Obst. and Gyn. Brit. Emp.*, 1909, xvi, 84) concludes from the examination of 700 specimens of fibromyomas: (1) The menopause does not bring a cure to fibroids; on the contrary, increasing age increases the danger from these growths. (2) There is little danger of malignancy arising in fibroids before forty years of age, after which time the danger increases with each year. (3) In view of the sarcomatous changes, carcinomatous associations, and other degenerations of uterine fibromyomas, early removal is indicated when they are of sufficient size to produce symptoms and cause the patients to seek advice. Small uncomplicated fibroids in young women do not require early treatment. (4) Thorough pathological examination should be made of all fibroids for evidence of malignancy. The tumor should be opened at the time of operation and examined for adenocarcinoma or sarcoma. Particular study should be devoted to those tumors which are necrotic, cystic; or both, as among these are found the largest proportion of malignant changes. (5) In view of the large percentage of inflammatory changes in the Fallopian tubes and appendix, these should be examined at the time of operation, and removed if diseased.

**Some Difficult Cases of Urinary Fistulæ in Women, with Remarks on Prophylaxis and Treatment.**—Under the title given R. WORRELL (*Jour. Obst. and Gyn. Brit. Empire*, 1909, xvi, 99) reports several cases illustrating several varieties of urinary fistulæ in women, upon whom he had successfully operated by the plan devised by Colles and described by that celebrated surgeon in *Dublin Medical Journal*, of May, 1861. Worrell claims that the credit for devising this flap-splitting method should be, but usually is not, accorded Colles.

**Ovarian Displacements.**—C. H. STRATZ (*Ztschr. f. Geburt. u. Gynäkol.*, 1909, Band lxx, Heft 2, 283) concludes from his observations that displacements of the ovary are dependent upon an inherited or acquired lengthening of the infundibulopelvic and ovarian ligaments, as well as an extraligamentous position of the ovary, and are caused directly by mechanical injury and by changes in the anatomical relations of the pelvic viscera. Anterior displacements are very much less common than posterior displacements and complete prolapse. As a result of such displacements, there may be congestion, œdema, hemorrhage, and even oöphoritis and twisting of the ovarian pedicle. Recovery is commonly spontaneous, at times after simple reposition, and only exceptionally is operative procedure for the displacement as such necessary. Stratz considers the disease described by various authors as œdema of the ovary as nothing more than a symptom of displacement or, especially, of a twisting of the pedicle of a displaced ovary.

**A New Kind of Gynecological Massage and Its Indications.**—RICHARD HOGNER (*Amer. Med.*, 1909, xv, 408) describes a new kind of gynecological massage he is using for non-inflammatory pelvic diseases that is applied as follows: The patient lies on a double inclined plane about eighteen inches above the floor, the head and chest being comfortably elevated, the abdomen and the legs very much raised, thus getting the best relaxation of the abdomen and moving the intestines away from the massaging. The operator sits at the patient's left side, on the hard couch, his left hand and forearm in the median line of the patient, the elbow resting on the couch. Examination and massage are now made by the Brandt system, except after a short preliminary use a motor vibrator is used on the abdomen.

**Results of Operation for Cervical Carcinoma.**—PAUL REINECKE (*Ztschr. f. Geburt. u. Gynäkol.*, 1909, lxx, Heft 1, 130) has compiled the results of operation for carcinoma of the cervix uteri in the Würzburg University clinic from 1889 to 1907. Of the 526 cases appearing at the clinic, 215 were deemed operable and 311 inoperable. Total extirpation by the abdominal route was performed 66 times and by the vaginal route 142 times. High amputation of the cervix was performed 6 times. The primary mortality by the vaginal route was 12.67 per cent. Of 120 cases of complete vaginal hysterectomy operated upon previous to 1903, 16 died as the result of operation, 11 were lost track of or died as the result of other diseases, 62 had a return of the growth, and 31 were free from return after 5 or more years. A cure was therefore effected in 33.33 per cent. of the cases. In 77.42 per cent. of the return cases the condition was apparent during the first year after operation. The primary mortality by the abdominal route was 21.21 per cent. Of 27 cases operated upon previous to 1903, 7 died as the immediate result of the operation, 13 had a return of the cancer, and 7 remained well after five or more years. The percentage cured was therefore 35. Of the 6 cases of amputation of the cervix, 4 remained free from return and 1 was lost to view. The percentage cured was therefore 80. Combining the results obtained by the three methods, it appears that 42 out of 118, or 35.6 per cent., remained free from a return of carcinoma after five years, which comes very close to the results reported by Schauta, namely, 38 per cent.

**Ovarian Papillary Adenocarcinoma with Polypoid Metastasis in the Endometrium.**—L. ARZT (*Ztschr. f. Geburt. u. Gynäkol.*, 1909, Band lxx, Heft 1, 76) reports a carefully studied case in which a malignant papillary cyst of the ovary was believed to be the primary growth and a polypoid tumor in the cavity of the uterus the secondary growth. Both tumors had the same histological characteristics; the uterine tumor was not found to have any histogenetic relation to the mucous membrane of the uterus; and carcinoma cells were found within the veins of the uterus. Arzt believes that the growth was conveyed by way of the veins from the ovary to the uterus. He finds only three or four similar cases in the literature.

## DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES.

UNDER THE CHARGE OF  
J. SOLIS-COHEN, M.D.,  
OF PHILADELPHIA

**Albuminuric Coryza.**—CORNET (*Annales des maladies de l'oreille, du larynx, du nez, et du pharynx*, October, 1909) describes an albuminuric coryza, in which œdema of the pituitary membrane is the predominant element. He reports several cases, and states that he has found it one of the earliest symptoms of chronic nephritis, as verified by examination of the urine. The coryza itself yields to the constitutional antinephritic treatment.

**Paraffin Injections in Ozena.**—BOTÉY (*Annales des maladies de l'oreille, du larynx, du nez, et du pharynx*, November, 1909) discusses the question whether injections of paraffin in ozena are today the best treatment for this affection, and as the result of considerable experience with solid paraffin comes to the conclusion that this is really the best treatment. His results have been 50 per cent. of cures, 35 per cent. of great amelioration, and 15 per cent. of slight amelioration. He states that a preliminary injection of water beneath the mucous membrane facilitates the subsequent injection of paraffin. His cures of ozena, or amelioration, continue intact for many years. In contrary cases he had to repeat the injections to reproduce the results at first achieved.

**Remote Advantages of Ablation of Adenoid Vegetation.**—POPP (*Annales des maladies de l'oreille, du larynx, du nez, et du pharynx*, October, 1909) states, as a sequence of ablation of adenoid vegetations, he has seen cured two cases of exophthalmic goitre, one glaucoma due to lesion of the fifth pair of nerves and not relieved by iridectomy, and one case of Addison's disease. He suggests that the persistence of the craniopharyngeal canal, the vascular communication between the pituitary cavity and the pharyngeal mucous membrane, the presence of an accessory pituitary gland encountered sometimes in the pharynx, might cause an alteration in the secretory function of the pituitary gland, and indirectly, by intermediation of the grand sympathetic nerve and of the spinal marrow, of the other glands of internal secretion.

**Rhinopharyngocele.**—BROECKAERT (*Revue hebdomadaire de laryng., d'otol., et de rhin.*, December 4, 1909) describes a typical, if not unique, instance of this rare affection in a male infant, aged eighteen months. The swelling had been observed at the left side of the neck at the age of two months, and it had progressed slowly and steadily until it had acquired the bulk of a medium-sized orange. It proved to be an aërocele, which could be entirely emptied by pressure and which became refilled with air upon release of the pressure. A protracted examination



revealed a very deep fossa of Rosenmüller upon the affected side. As the fossa of Rosenmüller is regarded as the remnant of the second branchial cleft, it was concluded that this rhinopharyngocle was derived from the same cleft, the two formations being but the two extreme sides of the same process. It was proposed to incise the pouch and resect the sac as completely as possible.

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**Acute Lacunar Tonsillitis.**—HAHN (*Annales des mal. de l'oreille, du larynx, du nez, et du pharynx*, October, 1909) claims a cure of this disease in from twenty-four to thirty-six hours by the following procedure: Lavage of each crypt with a warmed mixture of hydrogen dioxide, twelve volumes, and a boric acid solution, 3 per cent.; then an injection into each crypt thus cleansed of a solution of novocain, 2 per cent. and adrenalin, 1 to 1000; finally, insufflation of anesthesin or of orthoform over the entire surface of the tonsil.

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**Spontaneous Resorption of a Morbid Growth of the Larynx.**—GREENE (*Jour. Amer. Med. Assoc.*, November 6, 1909) reports the spontaneous "disappearance of a laryngeal growth, probably carcinoma, without treatment." The patient, aged fifty years, had a growth about the size and shape of a small grain of wheat attached to the upper and inner side of the left vocal band. It increased somewhat in size, and then suggestion was made to use tuberculin for diagnostic purposes, and, if no reaction occurred, to remove a fragment of the growth for examination, with the object of performing laryngotomy or even laryngectomy, should it be found to be carcinoma as its appearance indicated. The patient seemed to agree as to the probable diagnosis, but preferred to continue at his work as long as possible without operation. The tuberculin produced headache and dizziness, and was therefore discontinued, but the small dose used gave no sign of reaction either in the appearance of the growth or in rise of temperature. Four months later the patient appeared for reexamination, and there was no sign of the growth to be seen. [Could this have been a tuberculoma and absorbed even with the small dose of tuberculin? J. S. C.]

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**Epithelioma of the Larynx Removed Through the Natural Passage with the Electric Caustic Snare.**—GAREL (*Revue hebdomadaire de laryng., d'otol., et de rhin.*, September 18, 1909) reports a pedunculated epithelioma, weighing two and one-half grams, which he removed from the larynx of a man, aged sixty-two years, with the electric caustic snare. The eschar showed that the section had been made at the point of junction at the left aryepiglottic ligament with the posterior border of the epiglottis. Eight months after the operation there had been no sign of recurrence. [This is one of the rare instances in which endolaryngeal procedure is justifiable for the removal of malignant neoplasms. J. S. C.]

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**So-called Multiple Osteomas of the Tracheal Mucous Membrane.**—MUCKLESTON (*Laryngoscope*, December, 1909) presents a review of the published cases of multiple ecchondromas and osteomas of the tracheal mucous membrane, and reports two cases of his own. One, illustrated, shows a section of the trachea and cricoid cartilage with

ecchondrosis surmounted by flat plates of bone. [It has always seemed that this condition is one of the exemplifications in which disease of tissues produced premature senile changes. J. S. C.]

**Rhinopharyngeal Fibroma Fatal by Intracranial Extension.**—GAUDIER (*Revue hebdomadaire de laryngologie, d'oto-rhinologie, et de rhinologie*, October 23, 1909) reports this case in a child from whom, at eleven years of age, he removed a rhinopharyngeal fibroma with great difficulty after external access by resection of the upper jaw. Two years later the patient returned on account of profuse hemorrhage from the nose and the mouth, which had existed about a month. On examination, there was no trace of recurrence of the growth. Nevertheless, the patient died suddenly the same day of a violent hemorrhage. Autopsy revealed a voluminous extension of the tumor saddling the sella turcica and raising the dura mater, and penetrating one side into the thickness of the sphenoid bone. The report of the case is followed by a resume of a few similar cases on record.

## HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF

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**Tuberculosis.**—The *Transactions of the Sixth International Congress on Tuberculosis* contain much valuable material which will be of the greatest service in the campaign against this disease. From the special lectures we make the following abstracts: Kitasato, discussing tuberculosis in Japan, shows the awakening of that nation and its active participation in the affairs of the world, at first developed factors which added to the increased spread of infection. The development of industry, by bringing a large number of people together, often under unsanitary conditions, the frequency of communication, the unequal development and distribution of wealth, putting a wide gulf between the rich and the poor—all of these have contributed to the spread of tuberculosis in Japan. In 1890 the death rate from tuberculosis did not exceed 11.4 per 10,000, but by 1900 it had reached 18. In 1904 the government inaugurated certain measures against this disease, the most important of which are the following: Spittoons are provided in all places of assembly, schools, hospitals, factories, ship stations, theaters, amusement halls, hotels, etc. The spittoons contain some disinfectant, and no one is permitted to expectorate save in these receptacles. In all hotels the bedclothes must be covered with white sheets, which are changed with change in guests. When an occupant is suspected of being tuberculous the room must be disinfected before another guest can be lodged therein. Tuberculous individuals in hospitals and prisons are isolated. These regulations are already having a recognizable effect upon the death rate from tuberculosis.

Pannwitz, under the title of "Social Life and Tuberculosis," gave a most inspiring address. In this he points out that tuberculosis must

be placed in the first rank of the dangerous accessory phenomena of social life. "Every third death during the working period of life is caused by pulmonary tuberculosis; every other workman who becomes incapacitated must ascribe his condition to tuberculosis. What frightful destruction of human labor! What a loss in development! What clouding and destruction of human happiness! How much progress is arrested by this disease! How much physical and mental effort is cut off prematurely! How many hopes for the future are blasted! What an enormous aggregate of misery is caused daily in our family life! Verily, tuberculosis has become the scourge of mankind! At the beginning of the twentieth century it stamps its mark on our entire social existence. It has become in our age the social disease."

Two things are essential to the development of this disease—the bacillus and susceptibility. The former may come from infected food, but in the majority of instances is distributed from some infected individual and is inhaled by the recipient. The chances of infection are multiplied by the density of the population and by the occupation of closed spaces. Intimacy of contact is an important factor in the spread of the disease, and for this reason one member of a family infects the others, and the more crowded the habitation the more frequent is the infection. The inhalation of dust or any irritative particles open up avenues in the respiratory passages for infection. Among the poor and the ignorant living in crowded quarters the infection of one generally means the ultimate infection of all. Predisposition may be acquired or hereditary. Insufficient food diminishes resistance, and tuberculosis among the poor is to be combated by securing for them sanitary dwellings, nutritious food, and by instructing them in sanitary matters. Sanatoria must be provided not only for the treatment, but for the education of the tuberculous. In Germany about one fourth of the inhabitants are insured against disability. More than 1,500,000,000 marks have been paid into this fund. More than one hundred free sanatoria are in operation; more than 50,000 tuberculous workmen pass annually through these institutions, and an average of 75 per cent. return able to support their families. In 1886 the death rate from tuberculosis in Prussia was 31.4 per 10,000; in 1906 it had fallen to 17.26. "At the end of the twentieth century the social qualities of people will be judged by their relation to tuberculosis." Pannwitz quotes Laquer as follows:

"The fight against tuberculosis has strengthened the social sense of the people and has set fresh goals for altruism. It has focussed the effort of nations, social classes, employers and employed, physicians and laymen in a common social ideal. It has rendered the individual as well as the mass of the people, which at bottom are antisocial and egotistical, both capable and ready to help indulgently and companionably. It has called into being a new feeling by assembling in Germany more than 40,000 human beings every year in sanatoriums; or, in other words, united them in a common striving for hygienic perfection; it has taught those who are weary and heavy laden the workings of the state, of the parish, and of insurance institutions, by showing the monumental results accomplished; it has drawn the sting of capital and has freed the lower classes from the sense of being abandoned in their hour of greatest need and danger. Every improved and cured tuberculosis subject becomes a propagandist of social doctrines. The sight of

children departing from the railroad station to join vacation colonies in forest retreats or convalescent homes is inexpressibly touching, and acts like the reading of a gospel more powerful than the Sermon on the Mount."

Newsholme points out that the most potent factor in the decrease of tuberculosis has been institutional segregation, and this is especially true when advanced cases have been cared for. He says:

"The institutional treatment which it is claimed has played a predominant part in the past reduction of phthisis has been in the main the institutional treatment of patients who were disabled by sickness, rather than of earlier and less severe cases. This is not the occasion for discussing the evidences as to the relative infectivity of early and advanced cases of disease. There can, I think, be no doubt that advanced cases are more infectious than earlier cases. But no responsible administrators having regard to the prevention of tuberculosis will content themselves with the treatment of advanced cases. They will treat early cases in the hope of securing recovery of the patient; and intermediate cases in the hope of restoring a modicum of health, as well as of educating the patient so that he will no longer be a source of infection to his family and his fellow workmen."

Probably the most interesting thing in the paper on the "History of the Treatment of Consumption," by Williams, is his description of the graded work now imposed upon some of the patients at the Brompton Hospital. No work is permitted if the temperature is above 99°. In others the work is divided into the following classes: (1) Walking from one to ten miles a day. (2) Carrying baskets of earth or other material, and gradually increasing the load. (3) Using a small shovel. (4) A large shovel. (5) Using a pickaxe, and (6) doing this for six hours a day. In many of the German resorts graded climbing has been used in the treatment of incipient cases since the time of Brehmer, but the graded work at the Brompton Hospital is the first systematic application of this method of treatment, and it is interesting to know that it seems to work beneficially. It certainly relieves the monotony of institutional life.

Volashimiroff in his lecture on the "Biology of the Tubercle Bacillus," states that these organisms have accumulated the fats and waxes contained in their cells for their own protection. "Thanks to the presence of this precious wax, the bacillus of tuberculosis is relieved of the necessity of forming spores, which other organisms are obliged to form in order to survive the unfavorable contingencies of life."

In his brilliant lecture on "One Hundred Years of Phthisiology," Landouzy dwells upon the conflict between the unicists and dualists. For awhile the great authority, Virchow, who taught that phthisis and tuberculosis were different diseases, gave the lead to the dualists. The famous phrase of Niemeyer, "The greatest danger that threatens a consumptive is to become tuberculous," strengthened this error, which was finally overthrown by the discoveries of Villemin and Koch. The studies of Villemin from 1865 to 1869 are summed up in the sentence, "Tuberculosis is caused by a morbid germ capable of multiplying in the organism. The inoculation of tubercle does not act through any visible or palpable matter that enters with this pathological product, but through a more subtle agent which is contained in it, and which

escapes our perception." The "subtle agent" was detected and isolated as the tubercle bacillus by the painstaking labors and genius of Koch. Upon these discoveries the science of modern phthisiology has been developed.

In his lecture on "Tuberculosis in Animals," Bang states that a hundred years ago the cattle of Denmark were wholly free from this disease, which was introduced by importation from Switzerland, Germany, and England. The cattle of Norway, Sweden, and Finland became infected later, also from importations. The entirely healthy herds are those that multiply from their own breeding, while the disease is found when the farmers trade cattle and import animals descended from infected herds. Inbreeding does not develop the disease; it must be imported in order to find its way into a healthy herd. The tubercle bacillus is not ubiquitous. If it were, it would be impossible to have healthy herds in a village in which other herds were infected. It is living for long periods in enclosures, stables, etc., in association with tuberculous individuals suffering from open tuberculosis. Congenital tuberculosis in cattle has been found in from 0.5 to 1 per cent. of the calves examined in Denmark. This occurs, however, only when the uterus itself is tuberculous, or bacilli circulate in the blood of the mother. The majority of cows reacting to the tuberculosis test bear healthy young, and when these are removed from the mother they remain healthy. It is quite proper to apply this knowledge to children. Remove the child from the tuberculous mother and the tuberculous home, place it in healthy surroundings, and take care that it is not infected through milk, and it will continue healthy. When the udder is tuberculous the milk contains a great number of bacilli, and of course should not be used in feeding either calves or children. However, bacilli may find their way into the milk even when the udder is not affected. Under the most perfect conditions of stabling and milking, some dust, which may be infected, is likely to find its way into the milk. Cows with tuberculous udders should be killed, as they are not fit for either breeding or supplying milk. Annually about 700 such cows are killed in Denmark, but their number is less than one per thousand since there are in that country about 1,000,000 milch cows. Bang does not agree with Koch in his opinion concerning the harmlessness of the bovine bacillus to man. The infant is much more susceptible to the bovine bacillus than is the adult.

Want of space forbids abstracts from other valuable lectures in this series.

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ORIGINAL ARTICLES.

CERTAIN VASOMOTOR, SENSORY, AND MUSCULAR PHENOMENA ASSOCIATED WITH CERVICAL RIB.

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THE symptoms of cervical rib have attracted much attention of late years, and are discussed in the exhaustive papers of Keen,<sup>1</sup> Thorburn,<sup>2</sup> and Lewis Jones.<sup>3</sup> The nervous and muscular features are those which most often attract attention. Last year I saw two remarkable cases, one of which threw light on a very inexplicable condition of the arm, which I had described years ago.

Mrs. L., aged thirty-one years, a strong, healthy woman, was referred to me by Dr. Andrew, of Thame. There was nothing special in her family or personal history. For ten or twelve years she had noticed a pulsation above the clavicle on both sides, most marked on the left; the physicians who first saw her suggested the possibility of an aneurysm. What has troubled her of late has been that after using the left arm for a short time there is a sensation of numbness, sometimes of "pins and needles," and if she continues to work, the skin gets red, and the arm feels swollen and hot; then in a little while she is quite unable to use the arm, and even has dropped things from her hand. The condition has increased very much of late, and it is for this that I was consulted. When quiet and at rest the arm feels natural, and she can do the ordinary work with her fingers. It is only when she attempts to use the arm that

<sup>1</sup> AMER. JOUR. MED. SCI., 1907, cxxxiii, 173.

<sup>2</sup> Med.-Chirurg. Society's Trans., 1905.

<sup>3</sup> Quarterly Jour. Med., vol. i.

numbness and tingling begin; then if she persists, redness and swelling follow, and finally she has to give up work. She has become nervous about it, and two months ago she appears to have had an attack of unusual severity, in which she fainted.

She was a very healthy looking woman with high color, no cyanosis; the radial pulses were equal; above the clavicles there was pulsation, somewhat more forcible on the left side on which it extended from the outer end of the clavicle upward and inward toward the thyroid. It was very noticeable, and one was not surprised that it had been regarded as aneurysmal. There was no pulsation to be seen in the sternal notch. After exertion, and in the erect posture, the left supraclavicular space looked fuller than the right, and a marked pulsation occupied the whole of the lower triangle. On palpation, no definite tumor could be felt, nor could one grasp a vessel between the fingers, and yet the pulsation was marked and distinctly arterial. The swelling was a little tender; on deep pressure one felt a resistance suggestive of a cervical rib. On auscultation, there was a systolic murmur over the vessel on the left side, none on the right. The left arm looked smaller than the right. There was no wasting of the muscles of the hand. Sensation was everywhere perfect. After moving the arm up and down, and working the muscles, she complained that the skin felt prickly and numb, and a flush extended over it, but no swelling followed. This, she says, only comes on if she persists in using the arm. The heart's impulse was a little forcible, but the sounds were loud and clear. Dr. Sankey took an x-ray picture, which showed well-marked cervical ribs on both sides, curiously enough, the larger one on the right.

The special point of interest about this case to me was the explanation it offered of two very remarkable cases, one of which I showed at the Philadelphia Neurological Society.<sup>4</sup> I give here a brief abstract: A man, aged forty-eight years, always very healthy and strong, a carpenter by occupation, complained of inability to use the right arm, which had been gradually coming on for some time. When at rest and quiet, it felt perfectly natural, and all the ordinary actions of life could be done without discomfort. There was no pain, no numbness or tingling, and the hand and arm looked natural; but when he worked, or used the right arm for more than a few minutes, he began to feel an unpleasant sensation and numbness and great tenderness; the color of the skin changed, and the whole arm became congested and swollen. This would occur in a very few minutes, and the veins would stand out with great prominence. There was a general dusky lividity of the skin. If the exercises were continued, the arm became visibly swollen. At rest, the circumference of the thickest part of the forearm was eleven inches, after exertion twelve and one-half inches. At rest, the radial pulse

<sup>4</sup> Jour. Nerv. and Ment. Dis., 1888. p. 248.

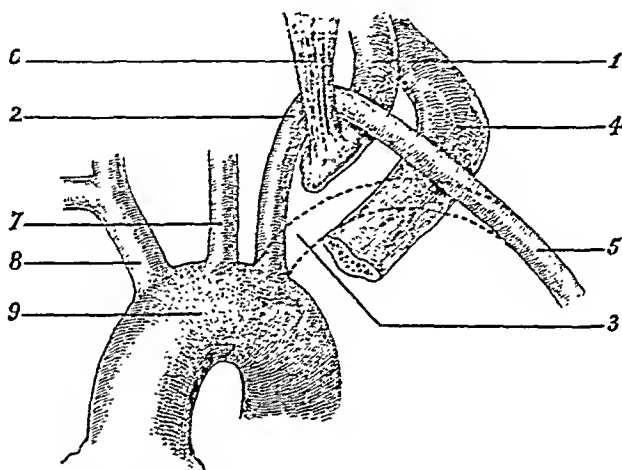
on the two sides seemed normal and equal; after exertion the right radial became very small, only just perceptible. When the arm was held up above the head, the congestion and swelling rapidly disappeared. Nothing whatever could be felt in the axilla, or in the course of the bloodvessels. I saw this patient at intervals of six months longer; he could do no heavy work, but all ordinary minor actions could be done without any swelling of the arm. The case was one that excited a good deal of interest, but no very satisfactory explanation could be offered. Unfortunately we did not at that time appreciate the importance of cervical rib, which I do not doubt was the cause of the remarkable disturbance in this case.

The other case was a woman, aged thirty-eight years, who came to my out-patient clinic at the Johns Hopkins Hospital, complaining of redness, pain, and stiffness of the right arm on exertion. At rest, the arm looked natural, but when used for ten or fifteen minutes there was a remarkable change—the skin became flushed, the fingers slightly cyanotic, and she complained of a feeling of stiffness with numbness and tingling, and if she continued to work the hand, the forearm became swollen and so stiff that she had to stop. There was no disturbance of sensation, no atrophy of the small muscles; the pulses were equal; there was nothing to be made out in the chest, or in the course of the arteries. I suspected at first pressure of glands high in the axilla, but nothing could be determined by the most careful examination. I did not think of cervical rib. The condition had persisted at intervals for several years and was the cause of great disability, as she could not work continuously for any length of time. If she did not use the arm there was no inconvenience.

In both these cases the symptoms, though more aggravated, were identical with those complained of by Mrs. L., and I have no doubt that, could we have taken x-ray pictures, cervical ribs would have been found. In Keen's paper several cases are reported in which the hand and forearm became livid and swollen. But it seems probable that there is a special group in which the symptoms come on only after exertion, and they resemble closely the condition known as intermittent claudication. In many cases the subclavian artery has been compressed in the angle between the rib and the scalenus anticus. When at rest, and with very slight muscular effort, enough blood reaches the limb, but the demand for more blood which follows exertion is not met, and there is stiffness and numbness with vascular changes. So marked may these latter be, that there are cases reported suggesting Raynaud's disease, and Keen states that in at least seven instances local gangrene has followed.

An important suspicion was raised in this case as to the existence of aneurysm. As Keen remarks: "On the whole, the evidences of true aneurysm in most of the cases in which it has been reported are,

to my mind, by no means always convincing. Usually the diagnosis has been based on the strong pulsation, sometimes with bruit and thrill. In a few cases, as in my own, the artery has been found, at operation, moderately enlarged, or in one case (Murphy's) flattened. In several cases operation has, therefore, disproved the presence of the supposed aneurysm. The postmortem in Adam's case disclosed a cylindrical aneurysm. Bearing upon the history of pressure or tension of the artery as it crosses the cervical rib, it is significant in Fischer's (Braun's) case that when the arm hung down (pressure or tension) a bruit was present, and when it was held up (relief of pressure) the bruit disappeared."



Scheme to show the changed course and the consequent angulation of the subclavian artery when it passes over a cervical rib. The dotted line (3) represents the normal gentle curve of the artery. 1. Cervical rib. 2. Subclavian artery passing over the cervical rib. Note its high position, its angulation, and the likelihood of pressure by the scalenus anticus 6. 4. First dorsal rib. 5. Axillary artery. 7. Left carotid. 8. Innominate. 9. Aortic arch. (Keen.)

But unquestionably, in a few cases, dilatation of the vessel, a cylindrical aneurysm, or even a sacculated tumor, has been present. In the case here reported, though the pulsation was diffuse and suggestive, there was no evidence of aneurysmal dilatation. To the Infirmary for Nervous Diseases, Philadelphia, Rose D., aged nineteen years, an inmate of the Pennsylvania Blind Asylum, was brought for a supposed aneurysm of the subclavian. There were the local paralysis and atrophy which one now recognizes readily enough as characteristic of cervical rib. Over this, no doubt, the subclavian artery was hooked, as in Keen's diagram, which I here reproduce, as it shows this angulation and elevation. It explains the position of the swelling in these cases, and the high pulsation. In the case of the blind girl just referred to the swelling in the supraclavicular region was marked, and while the mass itself did not pulsate, the vessel could be readily traced, and there was a loud murmur heard along its course.

## THE FUNCTIONS OF THE PITUITARY BODY.<sup>1</sup>

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INFORMATION in regard to the physiological properties of one of the glandular bodies whose secretion supposedly enters directly into the bloodstream may be gathered in numerous ways: (1) We may observe the immediate consequences of injecting its variously prepared extracts, or we may more accurately attempt to simulate the action of the hyperfunctionating gland by repeated injections, by feeding, or by implantations. (2) We may, on the other hand, study the reverse conditions comparable to lowered glandular activity by observing the effects of total or partial destruction or extirpation. (3) We may approach the subject in a round-about way by observing the alterations in its histological appearance and activity which follow the removal or injury of one or another of the allied or interrelated glandular structures. (4) We may gain some further insight into its function by the changes which occur not only in conditions of disease, but also during certain unusual physiological states, such as pregnancy, hibernation, puberty, and the menopause.

Let us consider *seriatim*, certain of the facts which these several methods have disclosed in regard to the functions of the hypophysis—facts which are merely steps toward the ultimate goal of determining the chemical nature of the active principle or principles to which it owes its activities.

1. SIMULATED OVERSECRETION BY INJECTIONS, FEEDING, ETC. Through the interest aroused in the possible importance of the pituitary body as an active organ which followed Marie's early papers, studies by injection methods were made at various hands. As is well known, it was shown by Oliver and Schäfer that the glandular extract, even when raised to the boiling point, led to a rise in blood pressure, and later by Howell that this substance was confined to the posterior lobe of the gland—the pars nervosa and its epithelial investment. The pressor response following this primary injection was found to be more enduring than that produced by adrenalin and to be accompanied by a definite slowing of the pulse, which occurs even when the vagi are cut or atropine is used. Even on the first injection, however, there may be an initial depressor reaction, and this, on subsequent injections, may be the only response. It was subsequently brought out by Schäfer and Magnus that this active principle of the posterior lobe distends

<sup>1</sup> Read at the combined session of the American Physiological Society and Section K of the American Association for the Advancement of Science, Boston, December 28, 1909.

the kidneys and increases the flow of urine. It shows a further resemblance to adrenalin in dilating the pupil; and similar atheromatous changes in the arteries are said to follow the long-continued administration of either extract.

These responses to extracts of glands of lower animals have recently been shown by Halliburton, Candler, and Sikes<sup>2</sup> to hold true for extracts of the human gland, and, using Baumann's method for the detection of iodine, they have made the important observation that the hypophysis, though capable of secreting colloid, differs from the thyroid gland in being iodine free.

All similar physiological reactions have proved negative so far as the injection of anterior lobe extract is concerned. We have occasionally observed a slight pressor effect in partially thyroidectomized animals, but we have found that the most striking consequence of anterior lobe injection occurs as a thermic response in animals suffering from hypopituitarism, a rise of 2° to 4° C. in body temperature being not unusual.

With Dr. S. J. Crowe, the attempt has been made to study the effects upon nutrition of repeated injections, and it is our experience, in partial agreement with others, that the extract of the entire gland, or of the posterior lobe alone, administered daily over long periods of time, leads to progressive emaciation, often with marked degenerative changes in the spleen and central necroses in the liver. Similar evidences of autointoxication, it may be added, we have not uncommonly seen after operative removal of the gland.

No conclusive results were obtained by repeated daily hypodermic administration of anterior lobe extract in the several puppies subjected to this treatment. They rather tended to lose weight than otherwise, and this has been the experience of Caselli and others. Possibly in these investigations too large an amount of extract has been introduced, or some *pars intermedia* may have been included in the preparation. Likewise anterior lobe injections in animals in the cachexia hypophyseopriva stage failed in any striking way to postpone the outcome of a total hypophysectomy, though we have been somewhat more successful in tiding over this critical condition by heterotransplants placed in the cerebral subcortex.<sup>3</sup>

The necessity of clearly distinguishing between the properties of anterior and posterior lobes becomes very apparent in all of these observations. And this is no less true for the proper interpretation of the results of feeding experiments. Ingestion of the entire pituitary, as was shown by the experiments of Thompson and Johnston,<sup>4</sup> leads to a loss of weight by stimulating metabolism,

<sup>2</sup> Quarterly Journal of Experimental Physiology, 1909, ii, 229.

<sup>3</sup> Crowe, Cushing, and Homans, Quarterly Journal of Experimental Physiology, 1909, ii, 389.

<sup>4</sup> Journal of Physiology, 1905, xxxiii, 189.

an effect which in all probability can be attributed to the inclusion of the posterior lobe extract in the preparation which they employed.

Sandri<sup>5</sup> observed no effect upon the growth of young mice from a two months' feeding of the pars anterior of beef pituitary, whereas those similarly fed on posterior lobe substance showed a notable arrest of development. Positive results, however, have recently been obtained by Schäfer,<sup>6</sup> who found that the growth measurements in a series of white rats fed upon powdered anterior lobe showed a definite increase over the controls; and certain observations, at present being conducted by Dr. Emil Goetsch in the Hunterian Laboratory, tend to give support to Schäfer's observations, at least so far as the effects of anterior lobe feeding on the body weight and growth of partially hypophysectomized puppies is concerned.

As is true of other ductless glands, the effort to increase secretion by the ingrafting of heterotransplants, whether in spleen, bone-marrow, or elsewhere, has been disappointing, for, on the principle elucidated by W. S. Halsted, it appears that transplants "take" only when there is some physiological glandular deficiency; hence it is impossible to study the consequences of hypersecretion in this way.

Injection and feeding experiments therefore show: (1) That in the posterior lobe or its epithelial investment is a substance which raises blood pressure, dilates the pupil, causes diuresis, and, when given subcutaneously or injected over long periods of time, is likely to produce marked nutritional disturbances; and (2) that ingestion of the anterior lobe, at least in the case of young animals, appears to have some influence in stimulating growth, and that injection of its extract in states of hypopituitarism leads to a temporary pyrexia.

2. SIMULATED UNDERSECRETION BY TOTAL OR PARTIAL DESTRUCTION OR REMOVAL OF THE GLAND. Attempts at surgical removal have been made by various operative methods on various animal species and with seemingly variable results—to be explained doubtless by incomplete extirpation and the failure to control the surgical procedure by a careful examination of the infundibular region in serial sections in order to exclude the possibility that viable fragments have been left behind. Sir Victor Horsley's original statement, based on the supposedly total hypophysectomy in two dogs, that no disturbance follows the loss of the gland, has been given wide credence, and subsequent observations by Marienescio, Vassale, Fichera, Gley, and many others have not been sufficiently conclusive to modify this generally accepted view.

Paulesco, of Bucarest, however, in 1908, using an improved

<sup>5</sup> Riv. di Path. Nerv. e Mentale, 1908, xiii, 518.

<sup>6</sup> Croonian Lecture, Proceedings of the Royal Society, 1909, lxxxi, 442.



surgical approach to the base of the brain, succeeded in removing the gland in its entirety from 22 dogs and 12 cats, and found that its loss leads to a peculiar train of symptoms invariably followed by death in the course of two or three days.<sup>7</sup> In all of the animals which survived, viable fragments of the anterior lobe were invariably found postmortem at the base of the brain. He furthermore was led to believe that the mere separation of the stalk was comparable to a total hypophysectomy.

Since the publication of these observations in 1908 an article by Gemelli,<sup>8</sup> of Milan, has appeared, criticizing Paulesco's operative method and recording a series of operations on cats by an intra-buccal approach, with contrary results. Following Gemelli's procedure a number of these animals were operated upon a year ago in the Hunterian Laboratory by Dr. John Homans, and symptoms, in every way comparable to those observed in the canine, followed all complete extirpations.

It can be appreciated that observations of this kind, requiring not only an elaborate and delicate operation, but a thorough histological postmortem examination, not only of the other ductless glands, but of the infundibular region by serial sections, are not a light undertaking, and the histological corroboration of the operative results were neglected in the fifteen experiments carried out with Dr. L. L. Reford in 1908.<sup>9</sup> During the past year, in collaboration with Drs. S. J. Crowe and John Homans, a series of a hundred hypophysectomies was made the object of a more thorough investigation, the detailed report of which is forthcoming. These observations lend further support to Paulesco's main contention as regards the consequences of a total hypophysectomy, but they have brought out the fact that not only is the operation much more easily conducted in young than in adult animals, but also that the acute symptoms of cachexia hypophyseopriva do not set in in puppies until a period varying from ten days to three weeks after the operation. They have shown also that a stalk separation need not be fatal, for the epithelial lobe need not lose its vitality and the gland may become reattached in a nearly normal physiological relation to the infundibulum. Loss of the posterior lobe, furthermore, leads to no obvious disturbances in the animal's condition, whereas removal of the anterior or epithelial lobe—the posterior lobe remaining *in situ*—is equivalent to a total hypophysectomy.

The symptoms of cachexia hypophyseopriva are unmistakable, and, as has been indicated, set in after a variable period of from thirty-six hours to two weeks or so after the operation, depending upon the age of the animal. With the exception possibly of a

<sup>7</sup> N. C. Paulesco, *L'hypophyse du cerveau*, Vigot Frères, Paris, 1908.

<sup>8</sup> *Folia Neurobiologica*, 1908, ii, 167.

<sup>9</sup> Reford and Cushing, *Is the Pituitary Gland Essential to the Maintenance of Life?* Johns Hopkins Hospital Bulletin, 1909, xx, 105.

transient glycosuria, with or without polyuria, the animal in the interval appears perfectly normal in all respects. The onset of the symptoms is characterized by inactivity with a little stiffness and unsteadiness of gait and lowering of body temperature; an awkward arching of the back with incurvation of the tail is characteristic. In the course of a few hours or days, depending on the rapidity of progress in different ages, there is a further fall in temperature, together with slowing of pulse and respiration; and irregular muscular contractions occur, often with snapping of the jaw—coarse shivering movements which are not entirely unlike the tremors characterizing tetany. The animal becomes more and more lethargic and indifferent to his surroundings and finally lapses into an anesthetic state of coma, with slow pulse and an occasional deep diaphragmatic respiratory movement; and it is often difficult to tell just when life ends. Before this occurs the fall in temperature may have been extreme—to  $20^{\circ}$  C. or lower, almost room temperature.

In a series of hypophysectomized animals which have been observed this fall, Dr. Goetsch called attention to the fact that the heart is often found beating, or may resume its activity, when exposed post-mortem, and, like the batrachian organ, may continue to pulsate sometimes for half an hour after its removal from the body if placed in salt solution.

An examination of the other ductless glands from this series of animals has shown definite histological alterations, which are now under investigation. Some of the most striking changes have been observed in the thyroid and testis.

Our chief interest, however, has been centred in the animals who have survived the operation for long periods and in whom a postmortem examination has invariably shown that viable fragments of the anterior lobe have been left *in situ*, whether accidentally or, as in our later series, purposefully. These partial operations may be divided into three categories: (1) Those with removal of the posterior lobe alone; (2) those with a partial loss of the anterior in addition to the posterior lobe; and (3) those with total or fractional extirpation of the anterior lobe alone.

Owing to the persistence of a well-developed cleft, the posterior lobe in the canine is readily dislocated from the rest of the gland and can be removed as an intact fragment. As I have already stated, such a partial operation leads to no apparent disturbance in the animal's condition, though it must be admitted that fragments of pars intermedia which remain viable and possibly show hypertrophy are necessarily left adherent about the infundibular stalk in even the most complete operations. In these cases we have observed no striking post-operative alteration in blood pressure or urinary secretion, such as might be expected in view of the known effects of extracts from this part of the gland. On the other

hand, in those animals which have suffered a partial loss of the anterior lobe and have subsequently been observed for a long period of time, definite nutritional disturbances have frequently occurred. Thus, in puppies a partial hypophysectomy leads to a persistence of infantilism, and though the animals are fairly lively and playful, they remain undersized, acquire no secondary sexual characteristics, show a tendency to hypotricosis, often have a subnormal temperature, and are otherwise comparable to some of the clinical conditions to be described. Feeding experiments are being undertaken in some animals of this series.

In the adult animals subjected to a partial hypophysectomy other changes have been noted which suggest a reversion to the infantile type. A number of them have in the course of a few months become exceedingly fat, suggesting the experimental reproduction of the well-recognized clinical condition which accompanies certain cases of tumor of the hypophysis unassociated with akromegaly. In several adult males, furthermore, there has been a very evident atrophy of the external genitals, the tubules of the testis showing a tendency to reversion to the infantile type with loss of spermatozoa, absence of mitosis and other peculiar changes in the spermatogenetic epithelium, as well as certain alterations in the interstitial cells of Leydig.

Histological changes are also apparent in the thyroid and islands of Langerhans, and possibly also in thymus, adrenals, and ovaries, but we cannot speak definitely of these changes at the present time.

The view is a natural one that the glycosuria, for example, seen so often not only in the clinical cases of hypophyseal disease,<sup>10</sup> but also in these experimental conditions, may possibly be secondary to some alteration in the pancreatic islets rather than due to the primary hypophyseal lesion; and similarly that the adiposity may be consequent upon a testicular or ovarian disturbance comparable to the adiposity which follows castration or spaying.

3. HYPOPHYSEAL CHANGES SECONDARY TO LESIONS OF OTHER DUCTLESS GLANDS. Of these changes I cannot speak from personal experience, though alterations in the gland secondary to castration and to thyroidectomy have been described by various writers. Thus, the gland has been found to be uniformly larger, by measurement and weight, in castrated horses than in studs, and the same is true of cattle.<sup>11</sup> Gley demonstrated in rabbits that the gland enlarges after experimental thyroidectomy; Stieda and Rogowitsch

<sup>10</sup> Borchardt estimates (*Zeitschrift f. klinische Medizin*, 1908, lxvi, 332) that 35 per cent. of the reported cases of akromegaly have shown glycosuria, and on the view that the glycosuria might be due to hyperactivity of the gland he injected large doses of pituitary extract into dogs and rabbits, and in the latter glycosuria constantly occurred. This he interpreted as evidence that akromegaly is due to hyperfunction. We find that a temporary glycosuria, however, is a very frequent sequel of total or partial extirpations, so that a disturbance of carbohydrate metabolism may seemingly accompany either hyper- or hypopituitarism.

<sup>11</sup> Schütz, *Wiener med. Wochenschr.*, March 29, 1909, 606.

described the change as an hypertrophy of the anterior lobe, and Cimatori has shown that it is due to the loss of thyroid rather than parathyroid tissue. Herring,<sup>12</sup> however, finds the chief alteration in the pars nervosa, pars intermedia, and ependymal cells of the third ventricle.

That the reverse is true, namely, alterations in other glands secondary to hypophyseal lesions, we have abundant evidence, and it is just as natural that a lesion primarily involving some other of the family of ductless glands should bring about some functional readjustment which is productive of definite gross and histological changes in the hypophysis. The close physiological interrelation of all of these bodies, as emphasized by Falta, is most probable, and many illustrations may be drawn from conditions of experiment, as well as of disease. In the case of the hypophysis, however, just what the recognizable alterations signify awaits an interpretation which can only be forthcoming when we gain a more thorough knowledge of the exact physiological properties, particularly of the various cells which comprise the epithelial portion of this gland.

4. ALTERATIONS IN THE GLAND IN DISEASE AND IN VARIOUS STATES OF FUNCTIONAL ACTIVITY. Since Marie called attention to the association of akromegaly with hypophyseal tumors a number of phenomena in addition to the apparant relation of the gland to body growth have come to be recognized as frequent accompaniments of hypophyseal lesions.<sup>13</sup> Among these may be mentioned glycosuria, polyuria, impotence or amenorrhoea in adults, and the delayed or nonappearance of secondary sexual characteristics in the young; both of the latter conditions being oftentimes accompanied by a peculiar and occasionally an excessive degree of adiposity. Other less striking manifestations may occur, such as a subnormal temperature, hebetude, slowing of the pulse and falling out of the hair, with other cutaneous changes—all of them symptoms which, as we have seen, may appear in one or another of the experimental conditions already described.

The actual association of an hypophyseal lesion with akromegaly is by no means generally conceded, despite the obvious tumor or enlargement so frequently observed, for a number of autopsies of undoubted cases of akromegaly have shown a pituitary body which has been regarded as practically normal. Further confusion has arisen owing to the description of a group of cases by Fröhlich and others in which tumors in the infundibular neighborhood were accompanied by adiposity and infantilism in the absence of akromegaly.

<sup>12</sup> Quarterly Journal of Experimental Physiology, 1908, i, 28.

<sup>13</sup> We must clearly differentiate, of course, between the so-called neighborhood or pressure symptoms of infundibular tumors and the nutritional disturbances which are due to the direct implication of the pituitary body itself.

It is hoped that the experiments which have been briefly recounted will serve in a measure to clear away some of these obscurities, or at least establish a basis for further investigation. Doubtless an overactive gland may present but slight enlargement, or at least may show no definite tumor growth, just as hyperthyroidism need not necessarily be accompanied by any great increase in size of the thyroid gland. Certain surgical experiences in cases of akromegaly, notably a case of Hochenegg's, reported by Stumme, and a case of my own, with a measurable subsidence of the manifestations of overgrowth, suggest that this disease is actually due to overactivity of the pars anterior of the gland; and if Schäfer's recent feeding experiments are to be confirmed, they add further support to this view.

The persistence of the characteristics of infantilism in a number of our puppies subjected to a partial hypophysectomy, and the occasional evidence of secondary atrophy of the sexual organs, together with the appearance of adiposity in several of the adult animals, suggests that the cases in which an hypophyseal tumor has been found in common with symptoms of adiposity and either a persistence of sexual infantilism or a secondary sexual degeneration, point toward the lowering of hypophyseal activity as the explanation of this clinical syndrome.

Doubtless there are many border-line cases in which the symptoms are less outspoken, as is true of moderate grades of over- or under-activity of the thyroid; and it is quite probable too that some of the confusing cases of gigantism, or akromegaly, which become impotent or have amenorrhœa with more or less marked adiposity are cases in which a gland with primary functional hypertrophy has become transformed into the well-recognized malignant adenoma,<sup>14</sup> leading in the course of time to interruption of normal secretion with the production of symptoms which we recognize as being due to a lessening of the functional activity of the gland. In similar fashion myxœdema may replace hyperthyroidism. We have recently observed a patient with an hypophyseal tumor in whom a beginning adiposity with impotence indicated an existing state of hypopituitarism; but an x-ray of the hands showed unmistakable evidence of an unsuspected akromegalic change in the bones, presumably a relic of an earlier stage of the glandular disease which was accompanied by oversecretion.

This will, of course, be recognized as merely a rough working hypothesis which leaves many things unexplained, for considering these various phenomena as due to alterations of the pars anterior, it leaves the function of the posterior lobe largely out of consideration.

The epithelial investment of this lobe (*pars intermedia*: Herring)

<sup>14</sup> Löwenstein, Virchow's Archiv. 1907, clxxxviii.

is doubtless an important part of the gland, the function of which is not fully established, though the hemodynamic and other properties contained in extracts of this lobe are doubtless due to the secretory activity of these cells. Herring first called attention to the fact that their secretion in the form of hyaline globules, observable under the microscope, passes into the abundantly canalized tissue of the pars nervosa and could be traced upward until it emerged between the ependymal cells, to pass directly into the infundibular cavity of the ventricle. Our sections fully corroborate this observation of Herring's, and under certain conditions of experimentation we have seen the secretion greatly augmented in amount.<sup>15</sup>

With full acceptance of this view, therefore, it is but natural that conditions which cause a stasis of cerebrospinal fluid, such as hydrocephalus, whether of the primary or acquired type, will lead to a damming back of the secretion. This we have found to be the case. The pars nervosa is often overfilled with the hyaline globules, which may even be seen in certain sections in the infundibular cavity. Large retention cysts of colloid are often observed under these circumstances, but this material is basophilic and, so far as we have been able to tell from injections, it does not contain the active principle of the posterior lobe. It is not improbable that the hyaline globules which take an acid stain are chemically modified by their passage through the pars nervosa.

In almost all cases of brain tumor, whether associated with hydrocephalus or not, we have found morphological as well as histological evidences not only of this retention of posterior lobe secretion, but of pressure on the gland as a whole. This glandular deformation may be considerable, and varies from a slight cup-shaped depression to a scaphoid configuration of the gland, which may be compressed until it measures only two or three millimeters in thickness, with marked histological alteration in the cells, particularly those of the anterior lobe. It is not unusual for patients with either primary hydrocephalus or brain tumors to show a tendency to become adipose despite the serious nature of their underlying malady. It is well known also that amenorrhoea and impotence are common disturbances in tumor cases, and it is not improbable that these symptoms may be secondary to hypophyseal insufficiency such as we have described. This view has been advanced by Marienescio and others for conditions of hydrocephalus.<sup>16</sup>

<sup>15</sup> We have recently had the opportunity of studying the tissues from an excessively obese individual who died from the pressure effects of a large adenomatous tumor at the base of the brain. Dr. Crowe was fortunate enough, in studying a section through this growth, to discover a normal, though compressed, hypophyseal anterior lobe with undoubted evidence that the growth originated from the pars intermedia alone. The tumor resembled in its arrangement of acini containing colloid one which might have originated from the thyroid gland itself. The view has been advanced that the hypophysis may act vicariously for the thyroid, though there seems to be no justifiable grounds for this belief, as their extracts give quite contrary results, and the hypophysis, as has been stated, is iodine-free.

<sup>16</sup> Marienescio and Goldstein, *Revue neurologique*, 1909, xvii, 1000.

Before one can hope to interpret the pathological alterations of the hypophysis in disease, information is necessary in regard to its cellular appearance in different states of normal physiological activity, and this as yet has not been thoroughly acquired. There are three varieties of cells distinguishable by their variable staining reactions. The coarsely granular acidophile cells of the normal (resting ?) gland tend to lie in rows along the vascular sinuses. There occur also, in smaller numbers, large basophilic cells, while the centre of the columns or acini is filled with cells of an indifferent staining reaction—the *Hauptzellen* of the Germans. It is to be noted that the anterior lobe cells, as well as those of the pars intermedia under certain conditions (normal or pathological?), may secrete colloid, and this or a hyaline-like substance may even be seen within the blood sinuses of the gland; nevertheless, we must regard the cells of the pars anterior and the pars intermedia as differing widely in function, and there may, indeed, be more than one active principle in each division of the gland.

The coarsely granular acidophile elements were thought by Benda<sup>17</sup> to represent the active stage of the anterior lobe cells, a view supported later by Dean Lewis, who has made a most careful study of the histological appearances in a case of akromegaly unaccompanied by tumor. During the course of our experiments we have attempted to determine the histological characteristics of the glandular hypertrophy which would be presumed to occur in cases of survival after a partial removal of the anterior lobe, and it is our impression, from the study of these sections and from certain experiments made by Dr. Crowe upon the effect of pylocarpine administration in animals presumed to retain an active fragment of gland, that the large vesicular type of cell, largely free from granules, represents the active, or at least the discharged stage; the abundantly filled chromophile cells, on the other hand, representing a resting or storage stage which does not necessarily indicate great functional activity.

It is quite possible that Scaffidi<sup>18</sup> is correct in his view that the various anterior lobe cells do not represent stages of activity of one and the same cell, but that they actually have different properties. Erdheim and Stumme's recent studies of the histological alterations of the gland in pregnancy<sup>19</sup> might also be regarded as an argument favoring this conception, for in this condition it is the central cells (*Hauptzellen*) which appear to become active and to fill the cell columns at the expense of and with the relative disappearance of the chromophile elements, which remain few in number and instead of lining the sinuses are crowded to the centre of the columns. The distribution of these cells, as Dr. Goetsch has shown,

<sup>17</sup> Berliner klin. Wochenschr., 1900, xxxvii, 1205.

<sup>18</sup> Archiv f. microscop. Anat., 1904, lxiv, 235.

<sup>19</sup> Beiträge z. path. Anat. u. z. allg. Path., 1909, xli, 1.

is well brought out by the use of iron-hematoxylin stains, which pick out the chromophile granules in unmistakable fashion. We have had an opportunity of confirming these findings of Erdheim and Stumme's, and similar careful studies of a series of glands in other physiological states will doubtless show corresponding clean-cut alterations from the supposedly normal in the histological picture.

The weight of the hypophysis is somewhat greater in the female than the male, being slightly over 0.5 gram in the former and slightly under this weight in the latter. There is, however, a marked increase in the weight of the gravid gland, the particular specimen which we have had an opportunity of studying weighing 0.85 gram at the termination of pregnancy. The glands, on the other hand, from cases of intracranial tumor have been quite uniformly underweight.

Material taken at random from a series of indiscriminate autopsies has given us no special information of value. Through the kindness of Dr. Adolph Meyer we have had the opportunity of studying a series of 75 glands from the Worcester Hospital—a source similar to that from which Halliburton, Candler, and Sikes secured their material—and although histological alterations are present in the majority of them, it would be impossible to draw safe deductions without a thorough knowledge of the exact intracranial conditions and of correlating the findings with alterations in the ductless glands elsewhere from the same individual.

**SUMMARY.** It may be said that the pituitary body is a double organ in the sense that the secretion of its anterior and solidly epithelial portion discharges into the blood sinuses which traverse this part of the gland; whereas the hyaline substance, apparently the product of secretion from the epithelial investment of the posterior lobe, enters the cerebrospinal space by way of channels in the *pars nervosa*. Though possessing a physiologically active principle, as shown by the results of injections, the secretion of the posterior lobe does not seem to be so vitally essential to physiological equilibrium as that of the anterior lobe, the total removal of which leads to death with a peculiar train of symptoms which set in at an early date in the adult and after a longer interval in younger animals.

Alterations in the gland, which often ultimately assume the character of a malignant growth (adenoma) but which presumably, at least in their earlier stages, represent an hypertrophy, are common in clinical conditions of overgrowth (akromegaly and gigantism), and certain feeding experiments lend support to the view that these clinical states represent the consequences of hyperactivity of the *pars anterior*. Partial removals of the anterior lobe usually lead to obvious disturbances of metabolism accompanied oftentimes by adiposity and in the young by a persistence of infantilism, or in adults by a tendency to lose the secondary sexual characteristics



already acquired. These experimental conditions are comparable to those which have been recognized clinically as accompaniments likewise of tumors in the hypophyseal region, which under these circumstances can therefore be interpreted as lesions which through pressure have led to lessened glandular activity.

In view of the apparent interrelation of many of the glands of internal secretion it is quite probable that certain of the symptoms known to accompany hypophyseal disease may be consequent upon a secondary change in other glands which follows the primary lesion of the hypophysis. These changes are seemingly more outspoken and more widespread after a lesion of the pituitary body than after a corresponding lesion of any other individual member of the group of ductless glands, and in view of its unusually well-protected position one might have conjectured that it must represent a vitally important organ.

## AN ACUTE INFECTIOUS DISEASE OF UNKNOWN ORIGIN.

A CLINICAL STUDY BASED ON 221 CASES.

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FOR many years great confusion prevailed about the two diseases which are now known as typhus and typhoid fever, even after clinical knowledge of these diseases had separated them from the large group of "pestilential fevers" with which they had previously been confounded. This confusion was due to the fact that, irrespective of the lack of pathological investigation and the ignorance of the causative factors of these diseases, no well systematized analysis of the clinical features of them had been carried on. At the end of the eighteenth and the beginning of the nineteenth centuries the first great work on the differentiation of typhus and typhoid fevers was begun. We owe to Prost,<sup>1</sup> in France, the recognition of the intestinal lesions as the important distinctive lesion of typhoid fever. Even with the great contribution of Petit and Serres,<sup>2</sup> who followed and elaborated on Prost's work, showing that the lesion was limited especially to the lower part of the small intestine, and of Bretonneau,<sup>3</sup> of Tours, that the

<sup>1</sup> Médecine éclairée par l'observation et l'ouverture des corps, Paris, 1804.

<sup>2</sup> Traité de la Fièvre Entéro-mésentérique, Paris, 1813.

<sup>3</sup> De la maladie, à laquelle M. Bretonneau a donné le nom de dothiéntérique, ou de dothiéntérisme, Arch. gén. de méd., 1826, ser. 1, tom. x, 169. Notice sur la contagion de la dothiéntérisme, Arch. gén. de méd., ser. 1, xxi; also, de la dothiéntérisme, Arch. gén. de méd., 1826.

lesion was always localized in the agminated and solitary glands of the ileum, the great acumen of Louis,<sup>4</sup> who gave the name typhoid, and of Chomel<sup>5</sup> could not dissociate clinically typhus from typhoid fever. They all regarded the contagious fever of camps, of armies, and that of the English writers as identical with the disease whose lesion they so meritoriously discovered and analyzed.

Just as important as this was the work at differentiation being done in Great Britain by James Muir,<sup>6</sup> Edmonstone,<sup>7</sup> Hewett,<sup>8</sup> of St. George's Hospital, Bright,<sup>9</sup> Alison,<sup>10</sup> Craigie,<sup>11</sup> Cheyne,<sup>12</sup> who were able to support the findings of the French authors, but only in a limited number of the immense number of cases at their disposal. Thus, it came about that the French pathologists rarely failed to find the intestinal lesions, for they were dealing with typhoid fever cases mainly, and the English investigators, who were dealing with much the greater number of typhus fever cases, rarely found the lesion. In 1835 Peebles<sup>13</sup> pointed out to Perry<sup>14</sup> of Glasgow, the *rubeoloid* eruption of typhus which he had learned to recognize in the typhus of Italy. Perry, thereupon, in the following year in a paper, correctly described many of the differences between typhus and typhoid, and showed the absence of the rubeoloid eruption in "dothienenteritis," although Stewart who was present at the Glasgow hospital when Peebles demonstrated the rubeoloid eruption to Perry, insisted that Perry had maintained (even though Perry in his writings had not stated that "dothienenteritis" had an eruption of its own) the complete difference between the two eruptions. It was Lombard,<sup>15</sup> of Geneva, in 1836, who was the first to state definitely that there were in Great Britain two distinct and separate fevers, one of them identical with contagious typhus, the other a sporadic disease, identical with typhoid fever, or dothienenteritis, of the French. In Germany, however, as early as 1810, Hildenbrand<sup>16</sup> distinguished between the contagious typhus and the non-contagious *Nervenfieber*.

<sup>4</sup> Recherches sur la maladie connue sous les noms de gastro-entérite, Fièvre putride, adynamique, etc., Paris, 1829.

<sup>5</sup> Leçons de Clinique Méd., tom. i, Fièvre typhoïde, Paris, 1834.

<sup>6</sup> History of a Fever in the Suburbs of Paisley in 1811, Edin. Med. and Surg. Jour., 1812, viii, 134.

<sup>7</sup> Account of an Outbreak of Fever at Newcastle, Edin. Med. and Surg. Jour., 1818, vol. xiv.

<sup>8</sup> Cases showing the Frequency of Follicular Ulceration in the Mucous Membrane of the Intestines in Idiopathic Fevers, London Med. and Phys. Jour., 1826.

<sup>9</sup> Reports of Medical Cases, London, 1827, vol. i.

<sup>10</sup> Observations on the Epidemic Fever, Now Prevalent Among the Lower Orders in Edinburgh, Edin. Med. and Surg. Jour., 1827, vol. xxviii.

<sup>11</sup> Report of Cases Treated in Edinburgh Infirmary in 1832-33, Edin. Med. and Surg. Jour., 1834, xli; also Elements of the Practice of Physic, vol. i, Fevers, Edinburgh, 1837.

<sup>12</sup> On Epidemic Gastric Fever, Cyclop. Pract. Med., 1833, ii, 233.

<sup>13</sup> Observations on Petechial Fevers and Petechial Eruptions, Edin. Med. and Surg. Jour., 1835 vol., xliv.

<sup>14</sup> Observations on Continued Fever in the Glasgow Hospitals, Edin. Med. and Surg. Jour., 1836 vol. xiv; also, Letter on Typhus Fever, Dublin Jour. Med. Sci., 1836, vol. x.

<sup>15</sup> Études clin. sur les fièvres typhoïdes, Gaz. Méd., 1839.

<sup>16</sup> Ueber den ansteckenden Typhus, Wien, 1810.

To this country belongs the honor of definitely and firmly establishing the two diseases as distinct entities, owing to the epoch-making work and contributions of Gerhard and of Pennock,<sup>17</sup> of Philadelphia. They had studied in Paris under the great Louis, had been shown typhoid there, and on their return had investigated the disease in Philadelphia, but more especially an epidemic of typhus in Philadelphia in the spring and summer of 1836. They recognized the distinction between the disease of this epidemic and the typhoid fever in Paris demonstrated to them by the master clinician Louis. These observations were published by Gerhard in 1837, in February and August, and constitute the final differentiation between the two diseases. There is no chapter in the history of medicine more interesting and fascinating than the evolution of the clinical entities of typhus and typhoid fevers.

I have utilized this brief description of the course of the differentiation between these affections because it indicates how many workers in a field are necessary to establish the entity of any disease, the difficulty encountered, and finally the doubt which arises in many minds before final adjudication removes it. Bearing this in mind, I hesitate to submit the following theme which is based on an experience of 221 cases of an acute infectious disease which has probably for a long time, been considered by others as typhoid fever, but which I hope to show by definite clinical symptoms can have no relation to typhoid fever *per se*, but that it has a distinct clinical entity, entirely separate from typhoid, from typhus, or from any other disease known to me. My object in presenting this study is to enlist the attention of others who may have recognized the essential attributes of this disease, in the hope that by discussion the truth of my observations may be substantiated, or what would be equally advantageous to all, the error of my deductions be indicated.

There can be no doubt that the remarkable discovery of agglutinins by the work of Pfeiffer,<sup>18</sup> Durham,<sup>19</sup> Grünbaum, and that of Widal<sup>20</sup> in establishing the practical basis upon which serum reactions can be made in typhoid fever, has made the diagnosis of typhoid fever, by their demonstration in the blood, much more easy than before the discovery. Equally important with this reaction in simplifying the diagnosis was the establishment of the fact that typhoid fever is a bacteremia and is characterized by the presence of the Eberth bacillus in the blood, more or less constant, at all times of the disease. The practical application of cultural methods to recover the organism from the blood in this dis-

<sup>17</sup> On the Typhus Fever which Occurred at Philadelphia in 1836, Showing the Distinctions Between it and Dothienenteritis, AMER. JOUR. MED. SCI., February and August, 1837, vols. xix and xx.

<sup>18</sup> Zeitschr. f. Hygiene, Band. xxi.

<sup>19</sup> Prac. of the Royal Soc., vol. lix.

<sup>20</sup> Bull. méd., 1896.

ease, demonstrating its presence in over 90 per cent. of all early cases of typhoid fever, has been also of inestimable service in establishing the identity of typhoid and separating it from other bacteremias. Hence it is fair to assume that the recovery of the typhoid organism from the blood has much facilitated the diagnosis of the disease.

Everyone who has had considerable experience with typhoid fever and who has studied the voluminous literature of this disease has learned that the disease is so protean and complex in its clinical picture that at times a diagnosis can only be established with difficulty. Fortunately, deviations from the usual clinical picture are not common. There is a general congener of symptoms, however, whose existence establishes the presence of the disease clinically. While no one symptom may be said to be characteristic of the disease, there are two signs whose presence establishes the disease peradventure. Fortunately these two signs are the most constant, in fact, the only constant factors of the disease: (1) The presence of agglutinins which occur in over 95 per cent. of all typhoid fever cases; (2) the typhoid bacteremia, or the presence of the Eberth bacillus in the blood of patients suffering with this disease, which is constant in over 90 per cent. of cases.

It would seem to me that a clinician would be stepping on very thin ice were he to make a diagnosis of typhoid fever in the absence of the roseola, of the enlarged spleen, of the Widal reaction, of the typhoid bacilli from the blood, from the stools. and the urine, of the symptoms of intestinal ulceration, especially if the fever of the infection ran but a ten to fourteen day course. He certainly would find it well nigh impossible to prove his position. If this proposition be true, its corollary may also be assumed to be true, viz., that given a disease of definite duration, twelve to fourteen days, having a most extensive non-roseolar eruption, giving no clinical signs of intestinal ulceration, with the Widal reaction invariably absent at all times of the disease, with no organisms in the blood at any time during its course, and with a fever that falls by crisis, such a disease is most likely not typhoid fever.

It may be noticed in this argument that I have made no reference to a pathological basis of the disease I am about to describe, or to that of morbid anatomy. I wish I could, because knowledge from those sources might establish the truth, as occurred with typhus and typhoid fevers in England and France just one century ago. But in my study of the disease which forms the subject of this communication, I have not met with a single fatal case and therefore can offer no contribution to its pathology and morbid anatomy.

**HISTORY.** The theme, as may be inferred from these preliminary remarks, is based on a careful clinical study of 221 patients suffering from an acute infectious disease, and was begun late in 1896 and carried on since then. At that time, with a fairly large typhoid

fever service at Mount Sinai Hospital, I noticed a type of disease occurring mainly in the summer and fall months, somewhat similar, but characterized by many features irreconcilable to the picture of typhoid fever, such as the course (being twelve to fourteen days), the temperature descent, which was mostly by crisis, the eruption, which was maculopapular and did not disappear on pressure, and the absence of the Widal reaction in this group.

Widal had just published the agglutination test which is now known by his name, and we began our investigations with it. What struck me forcibly was the positive results we got with the typhoid fever cases and the invariably negative results with this group which we had separated clinically from these cases. Our investigation was further carried on during 1897. We attempted to recover, if possible, either a typhoid bacillus or some other pathogenic organism from the feces, the urine, and, even at that date, from the blood of the spleen obtained by aspiration puncture, but with negative results. The results of this clinical work were published by me in an article entitled "A Study of Seventeen Cases of a Disease Clinically Resembling Typhoid Fever, but without the Widal Reaction, together with a short Review of the Present Status of the Serodiagnosis of Typhoid Fever."<sup>21</sup>

With the limited material of this type of disease at my disposal at that time, my judgment as to the eruption was not as matured as it is now. I spoke of the eruption being roseola and disappearing on pressure. This was a mistake which I have long corrected, and was occasioned by the fact that there may be found here and there among the spots of the characteristic type of eruption, a few which may disappear on pressure. Since that time I have constantly and persistently watched for similar cases, and have collected up to December 1, 1909, from my service and my colleague's at Mount Sinai Hospital, 221 patients with the following type of disease. The most of these I have seen personally.

**DEFINITION.** An acute infectious disease of unknown origin and unknown pathology, characterized by a short incubation period (four to five days), a period of continuous fever, accompanied by intense headache, apathy, and prostration, a profuse and extensive erythematous maculopapular eruption, all of about two weeks' duration, whereupon the fever abruptly ceases either by crisis within a few hours or by rapid lysis within three days, when all symptoms disappear.

**GENERAL DESCRIPTION.** After a period of three or four days, during which the patient suffers from malaise, loss of appetite, nausea, and slight headache, the disease begins rather abruptly, many times with a chill or chilly sensation. This is followed occasionally by vomiting, by general body pains or pain in the

<sup>21</sup> N. E. Brill, *New York Medical Journal*, January 8, 1898, and January 15, 1898.

back; epistaxis sometimes occurs. The headache now becomes intense and apathy and prostration supervene with the rapidly rising temperature. The fever reaches its height in two to three days, when it remains constant thereafter, the temperature showing but slight diurnal remissions. During the fastigium of the fever the patient lies very quietly, sometimes moaning or groaning, with facial expressions of pain shown by the contracted and furrowed brow. His eyes are dull and suffused, his conjunctivæ congested, and his face, especially over the malar prominences, flushed. He is rather drowsy, his sensorium dulled, and he resents being disturbed by more marked expressions of pain; any attempt to move him increases his headache. The tongue is usually coated and moist, only occasionally is it dry and furred. The skin of the body feels hot and dry. The headache remains intense without diminishing in severity, and about the sixth day a rash appears. The eruption is found over the abdomen and back, and quickly spreads to the thorax and to the arms and thighs and occasionally to the neck, forearms, hands, legs, and feet. I have seen the whole body, even including the palms and soles, excepting the face, covered by the eruption. The rash is dull red in color, very slightly raised, and when subjected to pressure does not disappear. The individual spots on pressure fade slightly in color, and only very rarely can they be obliterated, but return to their florid efflorescence as soon as pressure is removed. The bowels are obstinately constipated, as a rule, and in many cases can only be moved by laxative agents. The pulse is full, rather slow, not nearly as rapid as might be expected with the pyrexia. It is soft and of low tension and often dicrotic. These symptoms remain in full development until about the twelfth day, when the fever abruptly disappears, the patient's temperature suddenly dropping in a few hours to normal, the rash fades, the headache leaves, the apathy and prostration vanish, and the patient feels perfectly well, taking an interest in his surroundings. A rapid convalescence follows. During the progress of the disease slight emaciation may develop, but rarely very marked. The urine is scanty, high colored, and at times contains albumin. Delirium is only exceptionally noticed, and then only at night in the patients with hyperpyrexia. A few patients show rigidity of the neck, and the presence in them of the Kernig sign may be elicited.

**ETIOLOGY AND ANALYSIS OF SYMPTOMS.** I have selected the histories of the last 50 cases of my series, chiefly because these histories were readily accessible and because I have had the symptoms tabulated for the purpose of comparative study. These 50 cases have come under my observation since June, 1906, and extend to December 1, 1909.

**Sex.** Males show a greater tendency to be affected than females. There were 34 males and 16 females.

*Nativity.* Inasmuch as the largest number of patients at Mount Sinai Hospital are Russians, Russia leads the list of cases with 30; Austria, 12; United States, 2; Ireland, 2; Germany, 1; not noted, 1.

*Month.* By far the largest number of cases occur in the summer months. Of this group there were 1 in January, 3 in February, 3 in March, none in April, 3 in May, 8 in June, 8 in July, 2 in August, 6 in September, 11 in October, 3 in November, and 2 in December.

*Age.* The disease is most common between the twentieth and fortieth years of life. In this group 33 appeared in that period: First to second decade, 9 cases; second to third decade, 19 cases; third to fourth decade, 14 cases; fourth to fifth decade, 4 cases; fifth to sixth decade, 2 cases; sixth to seventh decade, 2 cases. The youngest patient of this group was aged seventeen years, the oldest was sixty-five years.

*Contagion.* I can find no evidence of the disease being directly communicable. In the 221 cases we have not had, so far as I can learn, two members<sup>22</sup> of the same family, nor two from the same household or same house. The patients are admitted into the general wards, and the disease has never been communicated to any other occupant of that ward; nor has the disease ever arisen among the patients in the hospital. One of the nurses of the Training School who, in December, 1896, went through a severe typhoid fever infection, was attacked six months later with this disease, though at that time there was no other case of this disease in the hospital or training school. She was the only person I have seen developing the disease within the hospital.

*Food Poisoning.* It might be asked whether the disease has any relation to the ingestion of certain foods or to the toxins contained in decomposing food. The *prima facie* evidence seems to be against this view, for, if such were the cause, the disease would necessarily be widespread in special districts and affect many in a single family; secondly, the infection is not confined to any race, even though some races eat certain articles of food proscribed by others. We have found the infection in Germans, Americans, Austrians, and in the Celtic race. There is no analogy between this affection and the group of meat-poisoning cases known as botulism, and which seem to be due to the special organism of the Gärtner group—*Bacillus enteritidis* group. This group has the quality of interagglutinating, and its bacilli are often agglutinated by typhoid serum. In our examinations no such agglutination could be obtained. It seems highly improbable that a constantly definite and distinct type of disease, with unvarying type of eruption, running a definite course, subsiding at a definite period, and show-

<sup>22</sup> Since this was written I have had the opportunity to see at Bellevue Hospital, through the courtesy of Dr. Warren Coleman, four members of one family who were attacked almost simultaneously with this disease.

ing the character of this disease, could be due to a chemical ptomaine rather than to an infectious organized agent.

*Incubation.* The period, before the acute symptoms begin, varies in duration from sudden onset without premonitory symptoms to fourteen days. In 15 of this group of 50 cases the incubation period could not be ascertained, in 35 it varied from a few hours to fourteen days. The average of this stage of the disease was four and eight-tenths days. During it the patient suffered with malaise, fatigue, anorexia, constipation, dull feeling in the head or a distinct headache. Sometimes he complains of nausea and indigestion and painful sensations over the body. After this stage the disease in its intensity may be said to begin.

*Onset.* This may be sudden, when it is marked by a distinct chill, or chilly sensation, with increased general body pains or pains in the back, by nausea, and sometimes by vomiting. Now the headache becomes intense. Or the onset may be gradual, when it cannot be separated from the incubation period. In the latter case only the development of the fever and the increasing headache permit one to define this stage of the disease. In 19 cases the onset was sudden; in 31 the disease began gradually.

*Epistaxis*, while it occasionally occurs, is not common. It was noted during the course of the disease in three cases.

*Headache.* This is one of the most pronounced features of the disease and is almost invariably present. It may start in with the incubation or it may not appear until the onset. It becomes intense and at times agonizing, and in severity is only equalled by the headache of a meningitis, of a cerebral tumor, or the head pains occasionally present with syphilis. It lasts, as a rule, in all of its intensity throughout the disease, and then only disappears with the crisis. In the latter respect it differs from the headache of typhoid fever, which, as is well known, diminishes in intensity in the second week of that disease and is then no longer the chief subject of the patient's complaints. In this disease the headache is much more severe, and it lasts throughout its course until convalescence begins. The headache is general and is not confined to any locality of the head, being as severe in the occiput as in the frontal and temporal regions. In the cases in which the headache is most intense rigidity of the neck is sometimes observed; when the latter is present, a distinct bilateral Kernig sign may be observed. Rigidity of the neck and Kernig's sign were noted in four patients of this group. Lumbar puncture was made in these four patients, and the cerebrospinal fluid was examined culturally and cytologically. The growth was sterile in all, and the proportion of lymphocytes was slightly increased. The headache was agonizing in 8, intense in 33, and moderate in 9. With rigidity of the neck, there may be contracted pupils and, rarely, muscular twitchings and active reflexes.



*Facies.* The patients suffering with this disease look sick, much more so than a patient in the corresponding period of typhoid fever. The face is flushed, especially deeply over the malar prominences, the flush being, sometimes, not noted about the nose and mouth, which then may look unusually pale. The conjunctivæ are congested, the eyes suffused and later may become dull in expression. The forehead is wrinkled and the brows drawn together giving the expression of headache with which they suffer. The attitude in bed is generally relaxed, the patient being inordinately quiet. He does not toss about, as motion increases the headache. He resents being disturbed, and responds with reluctance to questions. He utters moans and groans and points to his head when asked where he suffers. It would seem to me that the physical relaxation and the indifference shown to the examiner represent an apathy which is only disturbed by an attempt to move him. This apathy is marked in most of the cases. In 6 of our group it was extreme, it was marked in 17, and absent in 12. In 15 the condition was not recorded.

*Prostration.* There can be no doubt, after one has seen a few of these patients, that this symptom is a striking one. It is marked by the general muscular relaxation, the posture of the patient in the bed, the indifference of the patient to his surroundings, and his lessened ability to move. It usually corresponds in intensity with the intensity of the infection, and is more marked with patients showing a hyperpyrexia than in the milder cases of the disease.

*Skin.* During the course of the disease the skin is hot and dry. Between the fifth and seventh day of the disease a maculopapular eruption appears, first on the back and abdomen and then over the trunk. The rash may spread rapidly, and in a great number of cases the arms and thighs may be covered. In a few cases the eruption involves, in addition, the neck, forearms, hands, legs, and feet, even exceptionally the palms and soles. At times the eruption is more profuse on the extremities than on the trunk. The eruption does not appear in crops, as in typhoid, but the spots appear synchronously over the area of the body which they invade. Each spot lasts throughout the rest of the course of the disease. It is noticeable that the rash is the most profuse when the attack is most severe. The spots are distinctly maculopapular, are only slightly raised and may be designated as an erythema. They are dull red in color. They vary in size from two to four millimeters, are uneven in contour, and are irregularly round or oval, their periphery being commonly diffuse and indistinct. If subjected to pressure they do not disappear, but fade slightly. This is best tested by pressing them with and under a glass microscopic slide, when all gradations of pressure effects may be observed. The eruption is more nearly morbiliform or rubeoloid than roseolar. In three of this group the eruption in places was distinctly petechial, suggesting a typhus fever eruption more than any other eruption.

From this description it may be seen that the eruption in no respect resembles that of typhoid fever, the eruption of which is characteristically papular, circumscribed and lenticular, appears in crops, very rarely involves the extremities, is never more profuse on the extremities than on the trunk, has never to my knowledge been observed to attack the palms and soles, and almost always disappears completely on pressure excepting in "hemorrhagic typhoid fever." The eruption of typhoid fever consists of hyperemic spots; in this disease it is distinctly erythematous, some of the capillary contents escaping into the surrounding tissues, leaving a more or less permanent zone which pressure cannot remove. I have looked for the subcuticular mottling of typhus, but have never observed it in these cases.

The eruption does not begin to fade until the crisis, then it rapidly becomes paler, and in two days thereafter only dirty yellowish-brown stains mark the site of the former spots. When petechiæ are present, the punctate hemorrhages disappear much more slowly. The rash is not nearly as discrete as it is in typhoid, for two or more spots frequently coalesce, a condition which is commonly seen. I have never observed the eruption on the face, but have seen it occasionally extend up the sides of the neck, involving the skin over the mastoids and even the back of the ear. Contrary to the typhoid eruption, which, as a rule, is not abundant, but occurs in varying crops of ten to twenty in number, this is, as a rule, an abundant eruption. In our series the following was the distribution of the eruption: Abdomen, chest, and back, 13 cases; abdomen, chest, back, arms, and thighs, 22 cases; abdomen, chest, back, arms, thighs, forearms, and legs, 9 cases. Distribution not noted, 6 cases. Of those with profuse rash involving the forearms and legs—9 in number—the eruption was observed on the palms and soles in 4, and on the neck in 3 cases.

*Herpes.* Labial herpes was noted as an accompaniment in 3 out of the 50 cases.

*Pulse.* The pulse rate, considering the fever, is not very high; it averages between 86 and 100 beats per minute. It is full, soft, and of low tension. Dirotism is not infrequently observed.

*Temperature.* The course of the fever is rather distinctive. The patients' temperature begins to rise at the onset, usually three or four days after the stage of incubation, and then with rapid strides, so that on the second or third day from the onset it may have reached its fastigium. It then averages between 103.6° and 104.2°. It is but slightly higher in the evenings, and continues high throughout the rest of the disease. The remissions between morning and evening seldom exceed 1° F. With the exception of these remissions the temperature remains constantly and uniformly high until the day before the critical fall, when a precritical rise may occur. In four of these 50 cases a precritical rise between

105° and 106° F. was observed. The precritical rise, however, is not the rule and only occasionally occurs. On the twelfth to the fourteenth day the temperature begins to drop. The fall is quick and abrupt, and in some of our cases within ten hours from 105° F. to normal. The critical fall occurs in a large number of the cases. In also a fair proportion of the group the temperature falls by rapid lysis (Figs. 1, 2, and 3). In this connection we have assumed as a standard by which judgment may be expressed the following: A crisis to be a fall in temperature to normal within twenty-four hours; rapid lysis to be a fall to normal in forty-eight hours; and lysis to be a fall to the normal within seventy-two hours. As a rule, after the fall, whether by crisis, rapid lysis, or lysis, the temperature does not rise again. Exceptionally a short rise, lasting but a few hours or a day thereafter, was observed. The most remarkable feature of this disease is that with the fall in fever all the signs clear up, and the patient, who may have felt and looked very sick, becomes alert, interested in his surroundings, and says he is well; the headache is dispelled, as if by magic; the eruption rapidly fades, and convalescence is established. In this group there was a critical fall in 16 cases, a fall by rapid lysis (less than forty-eight hours) in 17 cases, a fall by lysis in 17 cases. I have not seen a single patient whose temperature took more than sixty hours to fall to the normal, excepting with a complication.

*Eyes.* In 28 cases the eyes were suffused and the conjunctivæ congested; in 18 they were not affected; the condition was not noted in 4.

*Tongue.* The tongue is at first moist and coated with a white fur, the tip and sides remaining red. This condition may last throughout the disease, although in some of the cases with hyperpyrexia the tongue becomes dry and brown.

*Constipation* is a marked feature of the disease. It was present in 42; in 6 the bowels were regular, and in 2 there was a diarrhœa following a previous constipation. Very frequently the bowels can only be moved by the use of cathartics. Blood has never been found in the fecal discharges, either macroscopic or microscopic. The guaiac and benzin tests for occult bleeding have been negative.

*Tympanites* is not a feature of this affection. In 9 cases a slight abdominal distention was observed.

*Spleen.* This organ is frequently enlarged to palpation. In 27 cases of the series it was distinctly palpable below the costal margin. At times the spleen extends for a considerable distance below the ribs, four centimeters below being the maximum. In 16 cases it was one centimeter below; in 7 cases, two centimeters; in 2 cases, three centimeters; and in 2 cases, four centimeters.

*Mental Symptoms.* The apathy and dulled sensorium have been mentioned in the general description. Delirium is only

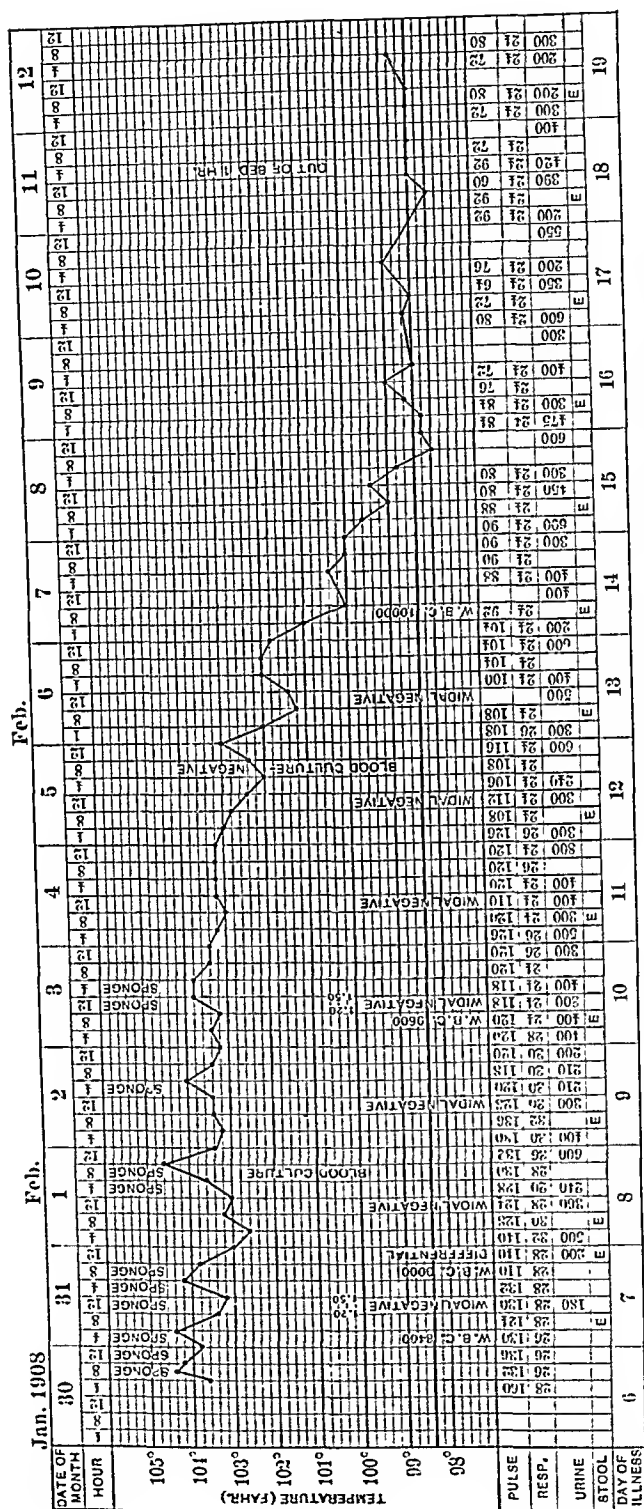


FIG. 1.—The temperature record, showing a fall by lysis within sixty hours, beginning on the thirteenth day.

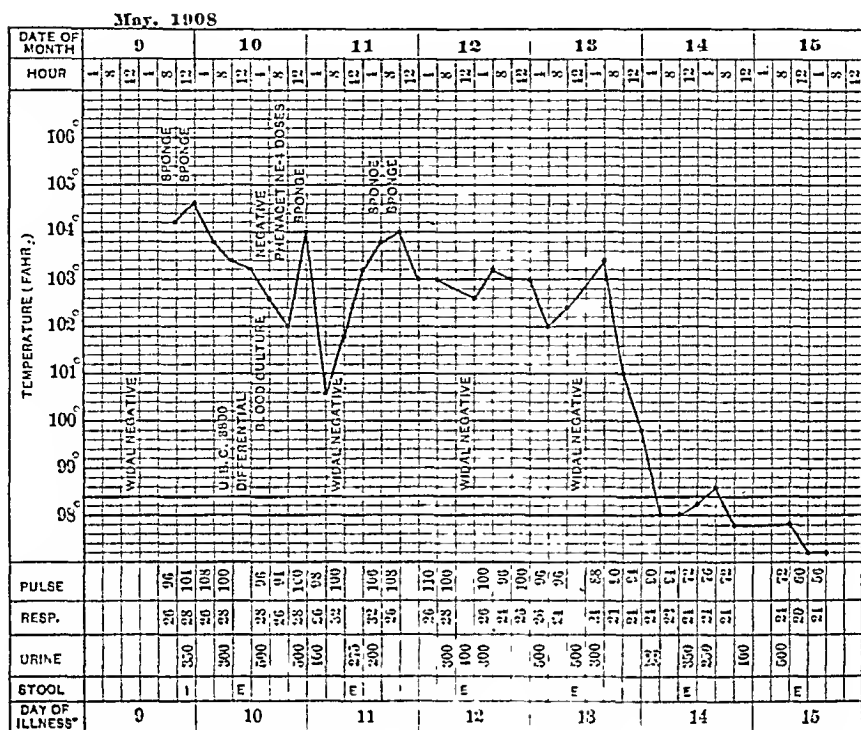


FIG. 2.—The temperature record, showing a critical decline (slight precritical rise) to normal within twelve hours, occurring on the thirteenth day.

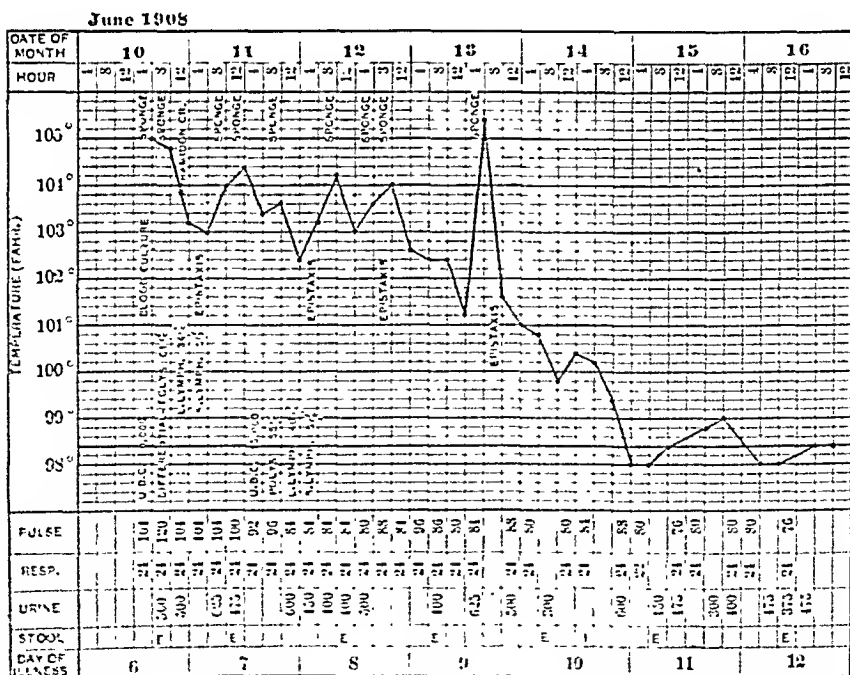


FIG. 3.—The temperature record, showing the precritical rise to 105° and decline by rapid lysis within thirty hours, on the ninth day.

occasionally present, and it does not assume the active type so commonly seen in typhoid fever. It usually occurs in those running a high febrile course, and then only at night. It is muttering in character.

*Blood.* The average white blood cell count is higher than it is in typhoid fever; there is not the tendency to leukopenia which typhoid fever blood shows, the count being between 9000 and 11,000. When bronchopneumonia exists as a complication the count is, of course, higher; our highest in such a case was 23,600. The average of the series—in only one case was no white blood count noted—was 9394, the lowest being 4200 and the highest 23,600, the last being in the patient with bronchopneumonia. The average count of polymorphonuclears was 69.4, and the lymphocytes, 30.6 per cent.

*Urine.* The urine is generally high colored and clear. It contains a faint trace of albumin in many cases and occasionally granular casts. Albumin was noted in 19 of the cases. The diazo reaction is not infrequently obtained, but it is more frequently absent than present. It was demonstrable in 9 cases, and no reaction could be elicited in 30; in 11 cases it was not noted.

**AGGLUTINATION REACTIONS.** In the 221 cases there has not been a single positive reaction to the Widal test. The test has been carried on perhaps much more assiduously than would have been the case had positive results been obtained. The blood has been sent to the laboratory daily in most all of the cases, not only during the course of the disease, but during the period of convalescence until the patient left the hospital. No positive reactions have been obtained. Tests were made in dilutions of from 1 to 20, and in some cases up to 1 to 1000, because it has been shown that agglutinations with the typhoid bacillus in some cases of typhoid fever are demonstrated only in high dilutions. Agglutination tests were also made in some of the cases with various paratyphoid bacilli, with several colon strains, and in a few cases with the Gärtner bacillus. The results were all negative. I believe that the absence of positive results speaks very strongly against these cases being due to infection by the typhoid bacillus or members of the intermediate group.

**BACTERIOLOGY.** The evidence of infection by the recovery of the offending organism in this disease is entirely wanting. Since 1896 we have persistently tried to isolate a specific organism from these cases, but without success. Blood cultures have been made in a very large number of the cases. During the past three years cultures have been made from all of the cases that have come under observation. The cultures in these cases were made under the direction of Dr. Libman. The methods used in this work during the past three years are the same as those that were used in the

studies of the bacteremia in typhoid fever made by Dr. Epstein.<sup>23</sup> Dr. Epstein obtained positive results in nearly all of the cases of typhoid fever. This makes all the stronger the proof that in the set of cases which I am describing we are not dealing with typhoid fever or paratyphoid fever.

The clinical aspect of the disease is strongly in favor of its infectious nature because it has a definite incubatory stage, one of onset, one of duration, and one of decline. We regard typhus fever, measles, scarlet fever, and the like as infections, and have no definite knowledge as to the nature of the infection, hence the absence of such knowledge as to this disease should not militate against considering it an infectious disease.

**PREVIOUS TYPHOID.** We carried on an inquiry based on immunity which typhoid fever gives to the one who suffered previously from typhoid, and found that in the group of 50 there were 10 who had had typhoid fever previously, 37 who had not suffered from typhoid fever, and 3 could give no information concerning previous illnesses.

If typhoid fever produces a short immunity, as has been shown, we would have a strong argument in favor of the cases here described not being typhoid, in the case of the nurse in the Training School, who had a severe typhoid infection in December, 1896, and who suffered with this infection in September, 1897.

**RELAPSES.** I have never seen a relapse in this disease. When the temperature once falls the disease ends. Unless there be a complication the fever does not rise again. This is so entirely different from the course of typhoid infections that in itself it would cast a serious doubt on the probability of this disease belonging to the typhoid fever group, with which some of my professional colleagues insist it belongs. They have stated in medical meetings that they see no reason why these cases should not be classified as atypical or abortive typhoid fever. I shall discuss this later in the section on diagnosis; for the present, however, I wish to call attention to the subject of relapses in abortive typhoid fever as presented by Dr. J. B. Briggs from Professor William Osler's clinic at Johns Hopkins Hospital. Dr. Osler<sup>24</sup> says: "J. B. Briggs has studied 44 of these mild cases from my clinic, in which the fever lasted fourteen days or less. Rose spots were present in 24, and the Widal reaction in 26. There were three relapses."

According to Murchison<sup>25</sup> and Curschmann,<sup>26</sup> relapses are especially prone to occur in the abortive type of typhoid fever.

<sup>23</sup> AMER. JOURN. MED. SCI., August, 1908, p. 190.

<sup>24</sup> The Principles and Practice of Medicine, by Wm. Osler, M.D., sixth edition, 1906, p. 91.

<sup>25</sup> A Treatise on the Continued Fevers of Great Britain, second edition, London, 1873.

<sup>26</sup> Der Unterleibstypus, Spec. Path. und Ther. (Nothnagel), Wien, 1902; also, American edition, with additions by Wm. Osler, Philadelphia, 1902.

With such a weight of authority as to the occurrence of relapses in abortive typhoid and the entire absence of relapses in this affection, one should at least be guarded in making positive statements as to the identity of this disease with typhoid infection.

COMPLICATIONS. *Bronchitis* is a common accompaniment of the disease and is present to a greater or less degree in the majority of the patients. When it develops, it is seen early, sixth or seventh day. It lasts as a rule, throughout and disappears in convalescence.

*Bronchopneumonia* was observed in 3 of the group.

*Meningismus*. What clinicians call signs of "serous meningitis," such as rigidity of the neck, contracted pupils, the presence of bilateral Kernig phenomenon, stupor, etc., are sometimes present. These signs were noted in four of the 50 of this group.

*Phlebitis cruris* was observed once.

*Otitis media* occurred in one patient.

*Cystitis* was observed twice, but I think it was due to some error in the technique of catheterization, which was done on both these patients.

DURATION. The disease lasts about two weeks. In our series the average duration was thirteen and three-tenth days. In one case it lasted five days and in one, twenty-two days. The last case, however, was accompanied by a bronchopneumonia and it was difficult to determine when the original infection terminated. The detail of the series is as follows:

5 days . . . . .	1 case	14 days . . . . .	5 cases
6 days . . . . .		15 days . . . . .	5 cases
7 days . . . . .	1 case	16 days . . . . .	2 cases
8 days . . . . .	1 case	17 days . . . . .	3 cases
9 days . . . . .	1 case	18 days . . . . .	
10 days . . . . .	2 cases	19 days . . . . .	1 case
11 days . . . . .	4 cases	20 days . . . . .	
12 days . . . . .	13 cases	21 days . . . . .	
13 days . . . . .	10 cases	22 days . . . . .	1 case

It will be seen from this that almost half the cases terminated between the twelfth and thirteenth days. This has been our experience with the rest of the 221 cases. A prediction may almost be made that the disease will terminate on one of the two days just stated.

DIAGNOSIS. To one who has had the features of the disease pointed out to him, the diagnosis is relatively easy. For the past few years the members of my house staff recognize the disease and make the diagnosis before my visit to the wards. This is also the case with the members of the "Admitting Department Staff" in the hospital. It is only on rare occasions that their judgment is found to be incorrect. It seems to me, if it be possible on first examination to predict, as it has been almost invariably, in these cases, that a patient having an eruption of this type will



not show at any time a positive Widal or give a positive blood culture, we are dealing with a disease *sui generis*. The positive factors of this disease which would suggest its presence when first seen by the examiner, are the facies, the headache, especially and definitely the eruption, the apathy, prostration, and the palpable spleen. It requires no great clinical acumen to differentiate the eruption, after its characters have been pointed out a few times. I have shown the eruption and along side of it in a typhoid fever patient, a roseola eruption, and the differences were so striking that the members of the house staff quickly learned to detect the differences.

**DIFFERENTIAL DIAGNOSIS.** Inasmuch as these cases have been considered by almost all my colleagues in New York, in the past, as typhoid fever cases, it will be necessary to show the marks of differentiation. The parallel column offers itself for this purpose as most convincing:

*Typhoid.*

*Unknown Infection.*

Usually long incubation.  
Onset not commonly abrupt.  
Fever; gradually increasing ascent of temperature to fastigium—in all about ten days.  
Remissions of temperature occasionally more than a degree.  
Fall usually by gradations to normal, taking commonly one week.  
Eruption, circumscribed, lenticular, papular.  
  
Distribution, chiefly, back and abdomen, seldom appearing on upper and lower extremities; almost unknown on palms and soles.  
Eruption appears in crops throughout the disease.  
Spots rarely confluent, and then confluence of but two spots.  
Roseola disappearing on pressure.  
Petechial spots (hemorrhagic) very rare.  
Apathy and prostration late in development.  
Labial herpes rare.  
Diarrhœa fairly common.  
  
Hemorrhages from the bowel often observed.  
Headache disappears in second week.  
  
Relapses observed by all observers.  
Widal reaction positive in over 95 per cent. of the cases.  
Blood cultures positive in over 90 per cent. of the cases.  
Convalescence slow.

Short incubation, four to five days.  
Commonly with chill or chilly sensation.  
Fastigium reached in three days.  
  
Rarely more than one degree.  
  
Fall commonly by *crisis*, not longer than sixty hours.  
Maculopapular, periphery indistinct and irregular.  
Distribution in addition to trunk on upper and lower extremities not infrequent, on palms and soles occasionally.  
  
Does not appear in crops.  
  
Confluence may occur with three or four spots forming a number of patches.  
Erythema, not disappearing on pressure.  
Petechiæ occasionally.  
Apathy and prostration early.  
Labial herpes in 6 per cent. of the group.  
Constipation an almost invariable accompaniment.  
No intestinal hemorrhages or blood in feces.  
Is more intense and lasts throughout the disease.  
Relapses have never occurred.  
Widal reaction invariably absent.  
  
Blood cultures invariably negative.  
  
Convalescence speedy.

*Typhus Fever.* In the case of an epidemic of typhus fever, in my opinion, it would be simply impossible to say that these cases which I have described were not mild typhus fever. From the

clinical aspects no lines of demarcation can be fixed. The onset, the eruption, though subcuticular mottling is absent, the critical decline, the absence of relapses are almost identical in both. If one can believe that typhus fever has been so modified by modern conditions of hygiene as no longer to be communicable, but to exist at all times in a community, to have lost its notoriously epidemic character, and to have been deprived of the grave nervous symptoms and its toxemia so as to be a non-fatal disease, then one could say that these cases deal with a modern typhus fever, or rather with a peculiar typhus fever which has been evolved by modern improved hygiene and sanitation. The preference of the disease for developing in the summer months is against the probability of its being typhus. Clinically this disease resembles typhus fever more than it does any other disease, and I should have felt that I had offered nothing to our nosology if it had been proved that typhus fever had lost its virulence, that it was constantly present in a community, that it was not communicable, that when it was present epidemics of it did not occur, and that it was no longer a grave and fatal disease. But with typhus fever, as the great masters of medicine have taught, and as I have seen it, such a conception would be unjustifiable; therefore, I believe this disease not to be typhus fever.

*Meningitis.* The occasional occurrence of signs of "meningismus" in this disease might suggest epidemic cerebrospinal fever ("spotted fever"). There would be no very great difficulty in determining the presence of that disease if spinal puncture were carried out and the cerebrospinal fluid examined culturally. Its cytology and bacteriology are definite, and the recovery of *Meningococcus intracellularis* would settle the diagnosis.

*Influenza.* In epidemics of this disease some cases might appear which have a great similarity to our disease. Those of us who dealt with the type of influenza as it appeared here in 1890 will no doubt recall cases very similar. The protean forms that were then observed would very likely suggest that perhaps this disease might be one of the multivariied or protean forms of influenza. Influenza appears pandemically, is very sudden in its onset, and prostration is the earliest symptom; it has no definite incubatory stage; it is accompanied by signs of cardiac weakness with rapid pulse and often with diarrhœa. It is par excellence the disease of complications and sequels, and especially of slow convalescence.

*PROGNOSIS.* Thus far it has been invariably good. No fatalities have ever occurred in my cases. Sick as the patients are and grave as the symptoms sometimes appear to be, one ought from this experience be justified in predicting a favorable issue to the disease.

*TREATMENT.* This for the present should be entirely symptomatic. Personally I have used no stereotyped plan. The usual remedies have been employed for the symptoms which required

relief. The diet has been restricted to fluid and soft nourishment. For the present I deem it wise, especially in cases occurring in institutions to use the usual precautionary measures which are employed in typhoid fever cases to prevent infection; nurses are so instructed in handling these patients. Such precautions, however, would seem to be unnecessary; nevertheless in the indefinite state of knowledge concerning the causative factors of this disease no injury can be done in using preventive measures.

EPICRITICAL. More difficult than separating this group from typhoid fever, among which it has been in all these years included, is the difficulty of giving a name to this disease. To my mind there can be no doubt that the clinical picture is so definite, so marked that it cannot escape recognition. If this should be the view of others, the disease must represent a distinct clinical entity. I am convinced it does and is entitled to a place in medical nosology. There is no sign in the clinical picture which would characterize the disease. The critical fall is definite and I thought it might be wise to use that feature for a provisional name, calling the disease "critical fever;" but pneumonia and typhus fever are likewise critical fevers. On this account the name is not desirable. I should emphatically deprecate calling the disease "pseudo-typhoid fever" because the affection has nothing in common with typhoid, paratyphoid, and typhoid-colon, or intermediate group infections. Some years ago, before we had done reliable blood work on this group, I believed that it might represent paratyphoid infections, and so I wrote,<sup>27</sup> but retracted that idea long ago, after I had convinced myself that the disease had nothing in common with paratyphoid. If it be typhus fever Health Boards should take cognizance of the fact that there exists in New York City at all periods of the year a non-fatal and non-contagious typhus fever which may possibly give rise at any time to an epidemic, though it has not done so in the last fourteen years. For the present, owing to ignorance of the pathology and etiology of the disease, I deem it wise not to give a name to the affection. I prefer to speak of it as an "acute infectious disease of unknown origin." My chief desire, in recalling to the attention of the profession this disease group, is to enlist its attention, in the hope that other observers may find similar or identical cases. Let us trust, if they do, that they can give us more definite and accurate knowledge than I have been able to offer. If this be the result of this contribution, or, if further inquiry shows that my attempt to establish a clinical entity has been based on poor observation and defective deductions, I should have almost as great satisfaction as would corroboration and additional proof bring to me, for it would have further and more forcibly taught me that while it is human to err, still truth will always prevail.

## A CASE OF THE ADAMS-STOKES SYNDROME OF PROLONGED DURATION, ENDING IN APPARENT RECOVERY.

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THE case which I report herewith, is that of an individual who has suffered from a number of prolonged attacks of complete auriculoventricular heart-block, and who made what for a time appeared to be a perfect recovery; but very recently (since the completion of this paper) he suffered a recurrence of the heart-block that lasted several days and then disappeared. So much has been written of late regarding the Adams-Stokes syndrome and heart-block that it is unnecessary to recapitulate all that has been learned regarding its etiology and pathology. Suffice it to say, that at present it is generally regarded as resulting from a complete or partial failure of the auriculoventricular bundle to conduct to the ventricle the stimulus to contraction which it receives from the auricle. As a result of this, the auricles beat more frequently than the ventricles, and, as might be supposed, marked disturbances in the arterial circulation occur and lead to the syncopal attacks and convulsive seizures which characterize the syndrome.

J. M. W. T., a male, aged fifty years. The patient's father died of angina pectoris; his mother died of carcinoma; one brother and one sister died in infancy. Four brothers and four sisters are living and well. The patient does not use alcohol; he uses tobacco, but not to excess. His bowels are usually regular. A specific history is absolutely negative. When a child he had chickenpox, mumps, and measles twice. He never has been seriously ill. He is subject to colds at times. He once was ill for three days with influenza several years ago. Most of his exercise was confined to walking and bicycle riding. On August 13, 1908, he came to me suffering from a neuritis of the left arm, which disappeared under the use of salicylates.

On November 19, 1908, having previously felt very well except for fatigue, he went to bed at his usual hour for retiring. Later in the night, in getting up to go to the bathroom, he suddenly lost consciousness for about one-half minute, and found he had dropped down on his knees. On arising he did not feel very weak, and went back to bed. Twice more during the night in getting up he fell to the floor, each time going back to the bed. There was no headache or nausea, but the patient vomited later, in the early morning. The bowels were regular, and urine had been passed during the night. I was called in to see him the next morning, November 20.

The patient before the attack was a well-developed man of medium stature, reddish-gray hair, florid complexion, well built, and with well-nourished skin. I now saw him quite pale, all mental faculties good, looking very ill. The pupils reacted normally, his tongue was coated, the arteries were fairly soft. The chest was well developed, the abdomen and extremities normal. Now and then, while answering questions, he would become very pale, the pupils would contract, the eyelids flutter rapidly, the eyeballs roll upward, the facial muscles twitch, and a general body convulsion would follow, the patient losing consciousness rapidly as the attack came on. The pulse would disappear at the wrist, and there was pulsation in the veins of the neck. Suddenly a faint flush would spread over the face, rapidly increasing in intensity. Following this there would be a return to consciousness, the patient looking rather bewildered, but soon he would take up the conversation again where he had stopped. The unconsciousness would last less than half a minute. The pallor would return gradually, but not to so marked a degree as before the attack. Occasionally he would vomit, but said there was no nausea, that the food would simply regurgitate. The pulse was 40 to 50 beats to the minute. After the convulsions the pulse would increase slightly in rapidity. It was quite strong and regular. After the attack the patient said he could feel the blood rushing through all parts of his body.

The heart dulness was apparently normal; the apex beat in the fifth interspace in the midclavicular line; the sounds were strong and regular; the pulmonic second sound slightly accentuated; a very faint systolic murmur was heard at apex, but was not transmitted. The liver, spleen, and lungs showed nothing abnormal.

The urine was acid, amber, cloudy, and deposited a moderate sediment. The specific gravity was 1012. Albumin was present and marked. Sugar was absent. Microscopically, amorphous urates, an occasional granular cast, and epithelium were found.

The attack continued all day with slight improvement. Toward night, the pulse rate was 50 to the minute.

During the day a series of convulsions and flushings would occur in the space of an hour; then no more for several hours. The vomiting also kept up until evening. About midnight he was more comfortable. The next morning the pulse had increased to about 60 beats to the minute. Through the day he had an occasional convulsion followed by flushes. One the third day, except for a very occasional flush, the patient was in a better condition. The pulse rate was now about 70. Convalescence continued uninterruptedly and by November 27 the patient had fully recovered, the pulse rate being 80 to 90, and the urine normal. The patient then went to Baltimore, where he underwent a thorough

physical examination by Dr. W. S. Thayer. All symptoms had cleared up and the heart was in good condition.

He then returned home and went about again as usual, except that he was careful in regard to exercise, until December 27, 1908.

*Second Attack.* On December 27, 1908, while at the telephone, he was suddenly seized with an attack, and fell to the floor. He had felt very tired for two or three days previous to the attack. I found his condition similar to the first attack. The temperature was subnormal, the pulse about 65 to 70; occasional flushes occurred. A nurse was called in and notes were made daily from that time until apparent recovery.

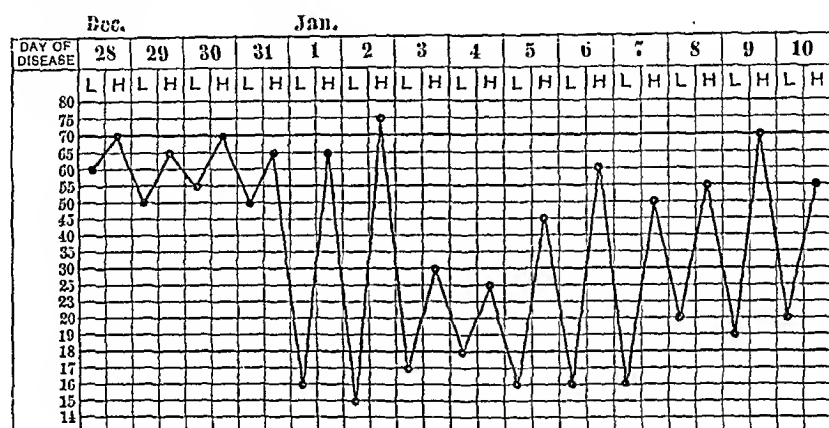


FIG. 1.—The pulse rate during the second attack. H, high; L, low.

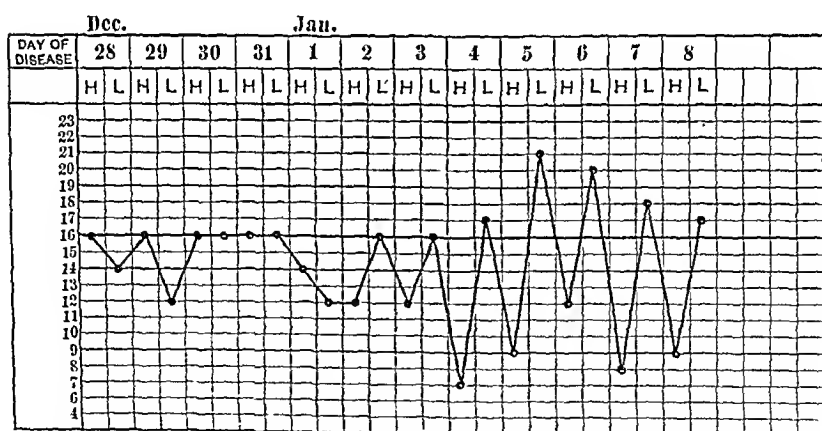


FIG. 2.—The respiratory rate during the second attack. H, high; L, low.

The patient was having what he called flushing attacks. On December 28 the pulse was 72 in the morning, the respirations 16, the temperature 97.3°. He was pale. Every little while his pulse would increase, then a flush would spread over the skin. The pulse would stop during the attack, then take up the normal beat. Arterial tension seemed increased. (Figs. 1 and 2.)

December 29. At 1 A.M. the pulse was 60. The patient was restless, wakeful, and had "flushing attacks." The pulse would beat regularly eight or nine times, followed by pauses of ten seconds, after which no acceleration of rate would occur. On December 30, his condition was much improved. After a comfortable night the pulse rate was 72.

On January 1, while sitting up, he had an attack of pulse intermissions lasting about half an hour, during which the arterial tension was high and the respirations slow and jerky. During this day the nurse's report shows that the pulse rate was very irregular; intermissions in the radial pulse lasting from four to twelve seconds were frequently observed. The pulse rate per minute ranged from 57 to 16, and the pulse waves were much fainter than heretofore. During the pauses pallor was extreme, the eyes fixed, the breathing slow and labored. When the pulse reappeared at the wrist a bright flush would spread over the face, and the pupils would contract and later again dilate. Curiously enough, the lips retained their color, and the hands their warmth during the intermissions, although the lower extremities were cold. During the intermissions the facial muscles would twitch and the eyeballs roll upward.

On January 2 the patient's condition was very alarming, pallor was extreme, the pulse very irregular, the skin was cold and clammy, and the patient was vomiting a yellowish liquid. One convulsion followed another, each lasting about twenty seconds. The jugular veins were prominent, and could be seen to pulsate more frequently than the radial pulse. On auscultation over the precordium feeble auricular contractions could be made out between the ventricular beats and during the long pauses. The ventricular sound was weak, the rate about 25 to the minute, while the jugular pulsations were ranging between 80 and 100.

The pulse in the right wrist was 63, without irregularity. The pulse of both wrists was taken together; the right was of larger volume. During the pauses of ten to twelve seconds, pallor was extreme, the eyes were set, the breathing was very slow and labored, not loud. The face became flushed when the pulse returned. The lips did not lose color, nor the hands warmth; the feet and legs were cold. The pupils were contracted after the flush, then dilated. During the pulse intermission the facial muscles twitched and the eyes rolled upward.

January 2, 1908. The patient's condition was very alarming. He was extremely pale. At this time the pulse became at times, very irregular. He started vomiting yellowish liquid, and was covered with a cold and clammy perspiration. One convulsion followed another, some lasting about twenty seconds. One could observe the jugular pulse in the neck, beating more rapidly than the radial pulse. The auricular contractions could be heard very

faintly, and the ventricular sound was also weak. The radial pulse was 25 to 30, the auricular beats about 80 to 100.

Drs. Alfred Stengel and William Pepper, of Philadelphia, and Drs. Thayer and Thomas, of Baltimore, were called in consultation and concurred in the diagnosis of heart block, positive proof of the condition being furnished by a pulse tracing made by Dr. Pepper. The patient's condition was still very alarming. Vomiting and convulsions kept up steadily. The pulse was weak and thready. After the convulsion the patient would complain of black specks flying before his eyes. Later on in the attack he complained of a lump in the stomach and cramps in the legs, which annoyed him considerably. Various kinds of treatment were administered, which will be discussed later.

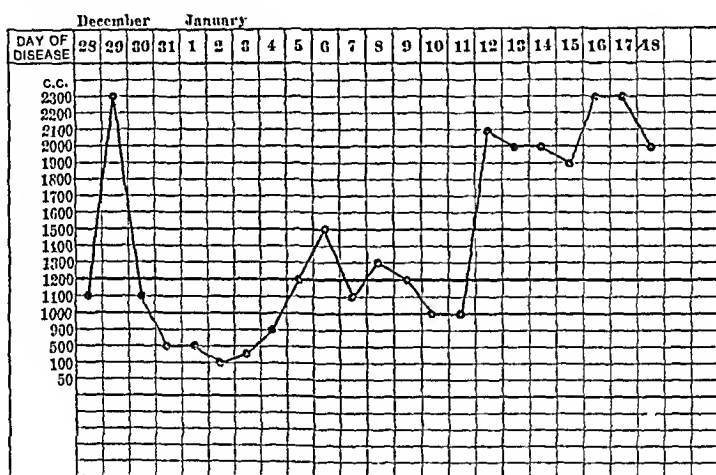


FIG. 3.—The amount of urine passed daily during the second attack.

At times the patient was excited and talkative on awakening. The secretion of urine at the beginning of the attack was high, but rapidly fell below normal for several days, then rose again (Fig. 3). Often during the attack the patient perspired freely. He suffered later in the attack from abdominal pain and distention, which gradually passed off. In his sleep he would jump and twitch, sometimes would mutter, talk, whisper, cry out, laugh, and pick at the bedclothes. The use of a bed pan would bring on convulsions, two of which were so severe he turned over from his back to his abdomen. The respiratory rate dropped as low as seven to a minute. Often the breathing became stertorous after convulsions, and sometimes was of the Cheyne-Stokes type. The temperature varied slightly during attacks, but remained subnormal. The pulse rate was sometimes 11 to 12 to the minute. The vomiting lasted until about January 6. At this date the radial pulse had reached 60, and there was a gradual, but steady, improvement.

On January 31 he was propped up in bed with pillows, and by



February 14 was sitting up in a chair. On February 21 he went to the Johns Hopkins Hospital, where he was under Dr. Thayer's care until about May 14. During his stay in the hospital he had several attacks, which will be reported by Dr. Thayer.

*Last Attack.* This attack began June 14, 1909, just about one month after his return from Baltimore, and lasted until August 8, 1909. Between attacks the pulse was ranged between 65 and 90.

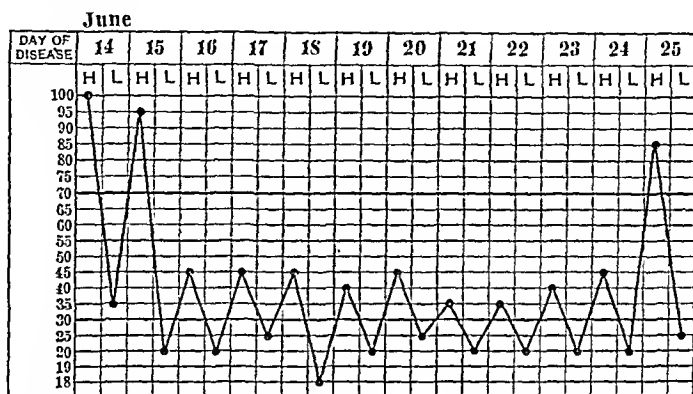


FIG. 4.—The diurnal variation of the pulse rate during the last attack. H, high, L, low.

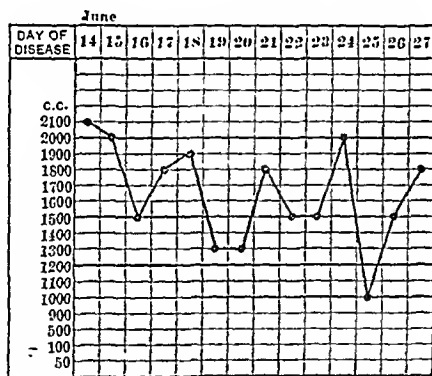


FIG. 5.—The amount of urine passed daily during the last attack.

After walking it would sometimes increase to 110 to 128 beats per minute. The treatment consisted of strychnine and infusion of scoparius. From June 14 to 23, during my temporary absence, he was under the care of Dr. George W. Norris and Dr. William Pepper. On June 13 the pulse was 88, the respirations 20, temperature 97.4° F. The next day at 6.15 A.M. the pulse dropped to 40. At times fifteen seconds would elapse between beats. The patient complained of pain in the abdomen and vomited at 7.45 A.M. After the vomiting the pulse became regular, 88 beats per minute. At 1.30 P.M. the pulse was 104. (Fig. 4 and 5.)

On June 15 (3.25 A.M.) there were *pauses in the pulse of ten to twelve seconds*. At 8.30 A.M. the upper and lower extremities

were cold. During this attack there was occasional vomiting. Very often after the vomiting the patient felt much relieved, and the pulse became stronger, but the rate remained unchanged. Often there would be an intermission in the pulse, followed by several very rapid pulsations. Once there was a period of unconsciousness lasting one minute. One of the convulsions lasting one-half minute, during which the face became purple, the mouth was drawn to the side, and eyes had a forced stare. On July 14 an erythematous rash appeared on the back, accompanied by intense itching, and on July 30 a similar rash again appeared. On each occasion he was taking strychnine. The patient during the most severe part of the attacks complained of red flashes before the eyes, which he said resembled tadpoles or question marks. He at times showed some depression just before attacks would come on. Even after the heart-block had subsided there was muscular twitching during sleep.

The patient passed through an uneventful convalescence. His weight from February 20 to August 14 had increased from about 165 to 192 pounds. There have never been any uncomfortable sensations referred to the heart. The pulse on December 16, 1909, was 88 per minute, regular, full, and strong. A faint systolic murmur was heard at the apex of the heart, but was not transmitted. The patient states that his hair, which had become rather white, has developed slightly more color, and that his skin has again assumed its normal rosy tint. At the present writing (December 16) he has apparently made a perfect recovery. Not only has he returned to business without any curtailment in ability to work, but a pulse tracing shows a perfectly normal heart action.

*Treatment.* During the first attack nitroglycerin was given,  $\frac{1}{200}$  grain every two hours. This drug was also used for a time during the second attack. There did not seem to be any effect from its use on the pulse rate. Potassium citrate was used during the first and second attack as a diuretic. Atropine ( $\frac{1}{150}$  or  $\frac{1}{200}$  grain) was given in the second attack, but did not appear to affect the radial pulse materially. On the first day of the last attack Dr. Norris ordered atropine,  $\frac{1}{60}$  grain, the dose being repeated four hours later. After the first dose the pulse remained at 24; when the second dose was given it rose to 90 beats. The pupils were dilated, the face was flushed, and the speech thick. At 9 P.M. the pulse again was 38 and the rhythm regular. Often during the attack the patient complained of uncomfortable sensations produced by atropine. Strychnine sulphate was used in all the attacks for its general tonic effect, but produced no noticeable benefit. Whiskey was employed for its stimulative properties, and I feel sure it had a good general effect. Morphine given hypodermically to quiet the patient, and for the relief of convulsions and vomiting, sometimes seemed beneficial. Oxygen was used

during the most severe part of the second attack, but as the relief produced by it was scarcely noticeable, it was discarded, as was also nitrite of amyl. Counterirritation to the epigastrium in the form of a mustard plaster failed to check the vomiting. Infusion of scoparius, which had been prescribed by Dr. Thayer, was continued for a time during the last attack, but did not seem to have either a beneficial or an untoward effect upon the heart-block. Quinine and caffeine were also tried. The effect of the latter is seen in tracings reproduced in Figs. 10 and 11. Massage seemed to improve the pulse volume temporarily and to add to the patient's comfort. Potassium iodide was tried and discarded. Aromatic spirit of ammonia had no effect on the heart-block. Cocaine and cerium oxalate were administered in an attempt to relieve the vomiting, without benefit. In short, none of the drugs employed seemed to have any effect on the heart-block, except in one instance in which large doses of atropine were temporarily followed by improvement. All medication was therefore stopped with the exception of an occasional dose of morphine.

The patient's condition remained unchanged, and on July 22 strychnine nitrate,  $\frac{1}{30}$  grain, was ordered thrice daily. The next day the pulse rate ranged between 30 and 80, the latter rate being higher than it had been for some time previously. This rate persisted for five days, and finally on the 28th the pulse rate was found continuously between 88 and 90 per minute. Strychnine nitrate was continued until the end of August and gradually withdrawn. After July 28 there was no further evidence of heart-block.

Whether the administration of strychnine nitrate had any direct effect in causing the heart-block to disappear, I am unable to determine. The patient had been taking strychnine sulphate, earlier in the attack, for a long time without any apparent benefit; but immediately following the administration of the nitrate the heart-block began to disappear in a most pronounced and dramatic manner. This may have been pure coincidence, and from what we know of the physiological action of these two salts it is hardly reasonable to assume that so much difference exists in their action as the results would seem to justify. That such a possibility exists, however, I think cannot be positively denied, and I would suggest that strychnine nitrate be given a trial in all cases of heart-block, so that the question of its efficacy can be more definitely determined. Too short a time has elapsed for us to be at all sure that another attack of heart-block may not at some future time occur. In view of the fact that the patient has already had, and recovered from, such attacks would be a reason for expecting just such an occurrence. On the other hand, it must be borne in mind that none of the patient's recoveries were as complete as this last one. Until now he has never felt well, he has had twitchings in his sleep, and occasional dropping of the pulse rate

to 60; whereas now he once more feels that life is worth while, he has resumed his occupation, his pulse is constantly within the range of normal variation; in short, for the first time since his first attack in 1908, his health seems to be completely reestablished.

*Report by Dr. George W. Norris on the pulse tracings taken by Dr. Pepper and himself:*

Fig. 6 (January 2, 1908) shows a complete heart-block. The auricle contracts from two to nine times as often as the ventricle.

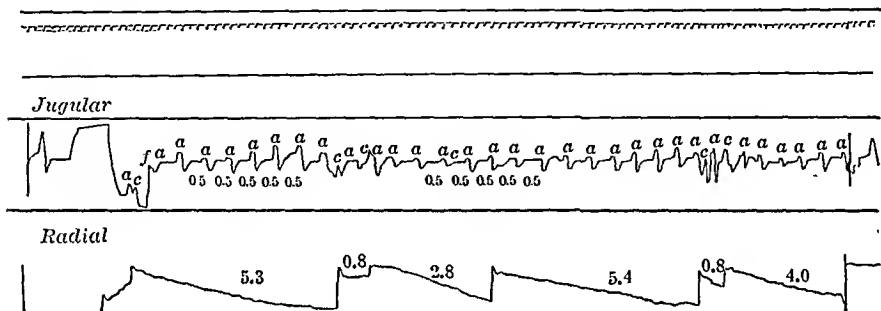


FIG. 6

Nearly 5.5 seconds elapse between some of the arterial pulses. The sinus rhythm (auricular cycle) is regularly 0.5 of a second. Two ventricular extrasystoles are seen on the tracing, conclusive proof that the excitability of the ventricle was not below par, and showing that the bradycardia was not due to depression of ventricular stimulability. Further substantiation of this statement is the fact that the block is a complete one, the auricular contractions therefore bearing no causal relations to the ventricular ones.

Fig. 7 (June 14, 1909) shows in every sense a normal state of affairs. Not only is there no arrhythmia of the brachial pulse, and

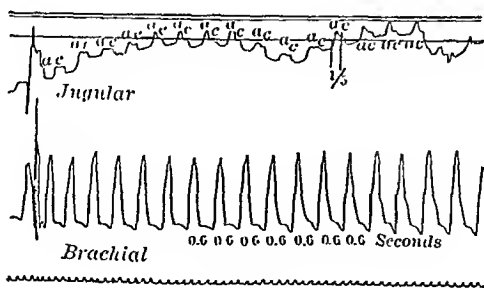


FIG. 7

no auriculoventricular dissociation, but the conductivity time—the *a-c* interval—is normal, occupying only 0.2 second. It has generally been believed that in cases in which the auriculoventricular bundle was sufficiently impaired in function to cause a temporary heart-block (even when the dissociation was not actually present),

a distinct lengthening of the time required for the contraction stimulus to pass from the right auricle to the left ventricle would exist. Such is, however, apparently not the case, as the foregoing tracing shows; for within twenty-four hours of the time when it was taken the patient was suffering from a complete continuous heart-block. We see, therefore, that the patient had at this time a normal auriculoventricular coördination; so that there can be no question of his having had an incomplete heart-block which had persisted since his previous attack, about two months ago. Such a state of affairs is possible, for incomplete heart-block may be present in unsuspected cases, and without giving rise to the symptoms which are characteristic of the Adams-Stokes syndrome.

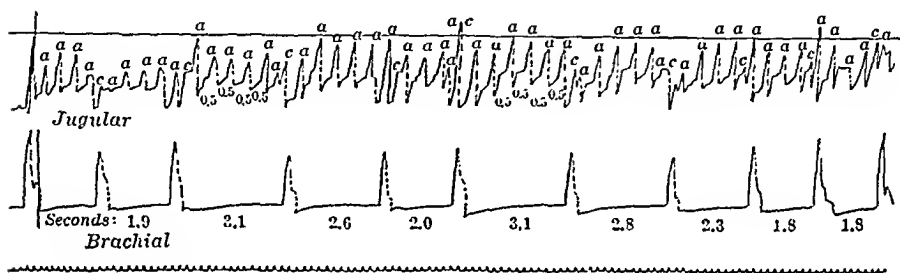


FIG. 8

Fig. 8 (June 15) shows a complete auriculoventricular dissociation. The auricle contracts from three to six times as often as the ventricle, and the contractions of these two chambers bear no constant or definite relation to each other. The ventricle has now initiated its own slow rhythm, and at one point in the tracing contracts at the same time as the auricle, producing a large summation or fusion wave. The radial pulse at the time this tracing was made was about thirty to the minute.

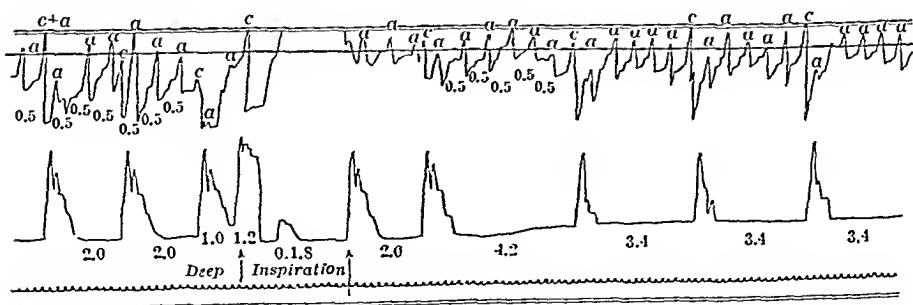


FIG. 9

Fig. 9 shows the effect of a deep inspiration upon the ventricular rhythm. The auricular rate was apparently unaffected (although during part of the time the tambour was forced beyond the tracing), but in the arterial pulse we find two extrasystoles following each

other in rapid succession, and then, after one normal ventricular contraction, a very prolonged pause (4.2 seconds); whether this change in the ventricular rhythm was from mechanical causes—due to an altered relationship between the intracardiac and intrapulmonic blood pressure—or whether it resulted from stimulation by the sympathetic nerve, it is difficult to determine. It is evidently not due to depression of the vagus nerve, since this nerve appears to act on the ventricles only secondarily to the auricles, and a state of block being present this influence of the auricles is excluded.

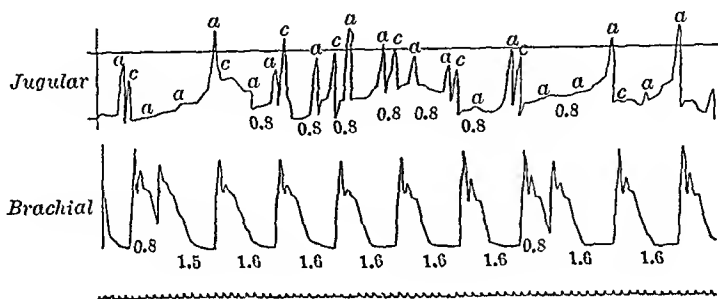


FIG. 10

Fig. 10 shows the complete auriculoventricular dissociation still persistent. The auricles are now contracting only about two or three times as often as the ventricles. On examining the time relationship of the auricular and ventricular cycles, we see that the former occupies 0.8 second, instead of 0.5 second, as in the previous tracings. The ventricular cycle, on the other hand, is diminished and requires only 1.6 seconds instead of from 2.0 to 4.2 seconds as heretofore. In other words, the auricular rate has diminished and the ventricular rate has increased. This was apparently the result of full doses of caffeine, which were administered to the point of producing wakefulness. Further evidences of increased ventricular excitability are seen in the occurrence of extrasystoles (two are seen on the tracing), which occurred very constantly during the next forty-eight hours. This result would seem to indicate that caffeine increases stimulus production and excitability in the ventricle. Further to be noted is the fact that the auricular cycle now lasts 0.8 of a second instead of 0.5 as heretofore. This is doubtless due to the withdrawal of the atropine, which, as is well known, increases the sinus rhythm by depression of the vagus nerve. On account of the patient's large chest and deeply placed apex beat, I was, unfortunately, at no time able to get a cardiogram, so that I was unable to study the presphygmie time, etc.

Fig. 11 shows the persistence of complete auriculoventricular dissociation and of the increased ventricular excitability—two-second intervals between arterial pulse waves and extrasystolic arrhythmia, producing a pulsus trigeminus and a bigeminus.

Fig. 12 shows that the extrasystoles have disappeared; radial pulse intermissions lasting from 1.8 to 4.4 seconds are again seen. Complete heart-block is still present.

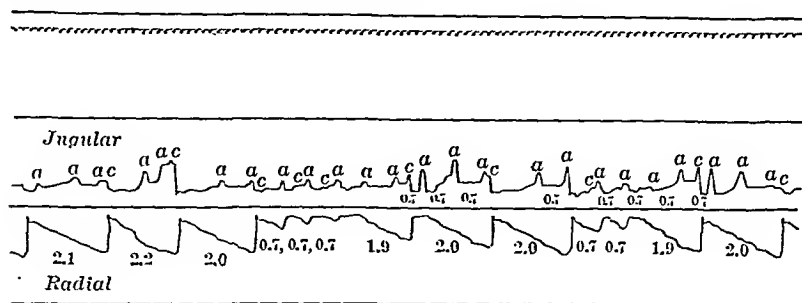


FIG. 11

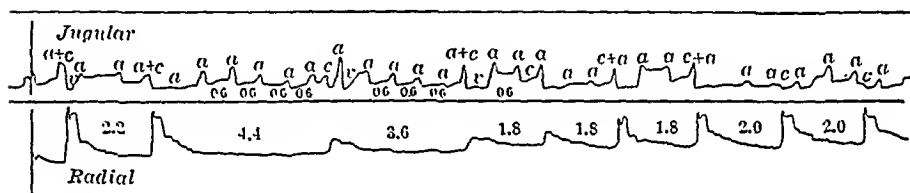


FIG. 12

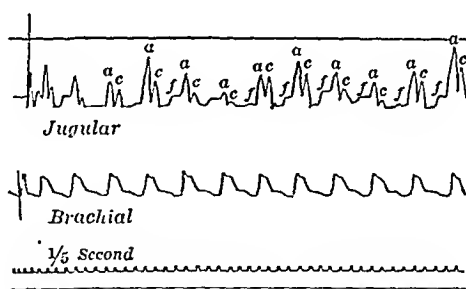


FIG. 13

Fig. 13 (December 15, 1909) was taken after a hard day's work, the patient being in good spirits and apparently in excellent physical condition. There is not only no auriculoventricular dissociation, but the conductivity time is normal, 0.2 second. The *a* wave in the jugular is perhaps a trifle larger than is usual, but otherwise no abnormality can be detected. The radial pulse was absolutely regular and 88 per minute.

It was quite astonishing to observe the way in which the blood pressure during all this attack had remained relatively near to the normal despite the enormous deviations in the rate of the arterial

pulse, yet this was uniformly the case, except on the day when the first tracing was made, in which the systolic pressure was very high and the diastolic very low. It should be stated, however, that I never happened to make a pulse tracing or take the blood pressure during those times at which the pulse was as low as 10 or 20 per minute. The lowest pulse rate which I had an opportunity of tracing was 24.

In endeavoring to explain this very extraordinary case, and elucidate the mechanism by virtue of which such a prolonged attack of complete heart-block could entirely disappear without leaving track or trace behind, in so far as our most exact methods can determine, we have indeed a perplexing task. The answer must necessarily be hypothetical until we possess a much more complete knowledge of cardiac physiology than is at present at our disposal. Quite a number of cases of heart-block have been carefully studied microscopically after death, and the following lesions have been described as being the cause of non-functionation of the auriculoventricular bundle: Fibrosis (Gibson,<sup>1</sup> Beeson,<sup>2</sup> Stengel,<sup>3</sup> Karcher and Schaffner,<sup>4</sup> Barr,<sup>5</sup> Fahr,<sup>6</sup> Turrell and Gibson,<sup>7</sup> Schmoll<sup>8</sup>), syphilis (G. C. Robinson,<sup>9</sup> Ashton, Norris, and Lavenson,<sup>10</sup> Hanford,<sup>11</sup> Vaquez and Esmein,<sup>12</sup> Keith and Miller<sup>13</sup>), fatty degeneration (Butler<sup>14</sup>), calcareous degeneration (Beck and Stokes<sup>15</sup>), thrombosis (Jellick, Cooper, and Ophüls<sup>16</sup>), atheroma of the vessel supplying the bundle with fibrosis (Hay and Moore<sup>17</sup>), ulceration,<sup>18</sup> atheroma of the vessel supplying the bundle and round cell infiltration of the bundle itself (Gerhardt<sup>19</sup>).

It is hard to conceive how organic changes, such as those just mentioned, could be recovered from, provided that they had been sufficiently extensive completely to destroy a cross-section of the bundle above its bifurcation or both divisions below this point, unless we are willing to accept the hypothesis that in cases of long-standing block the function of conduction can be assumed by parts of the myocardium other than the bundle itself, as was suggested by Heinike, Müller and Hösslin<sup>20</sup> in explanation of the second case studied by them. These observers suggest that inasmuch as the union between the auricle and ventricle is a very close one,

<sup>1</sup> Brit. Med. Jour., October 27, 1906.

<sup>3</sup> AMER. JOUR. MED. SCI., December, 1905.

<sup>7</sup> Brit. Med. Jour., 1906, ii, 1122.

<sup>8</sup> Brit. Med. Jour., November 14, 1908.

<sup>9</sup> Jour. Amer. Med. Assoc., February 3, 1906.

<sup>10</sup> Bull. Ayer Clin. Lab. of the Penna. Hospital, 1907.

<sup>11</sup> AMER. JOUR. MED. SCI., January, 1907.

<sup>12</sup> Presse méd., 1907, No. 8.

<sup>13</sup> AMER. JOUR. MED. SCI., May, 1907.

<sup>14</sup> Jour. Amer. Med. Assoc., 1906, p. 955.

<sup>15</sup> James, AMER. JOUR. MED. SCI., 1908, cxxxvi, 469.

<sup>16</sup> Deut. Arch. f. klin. Med., 1908, xciii, 5 and 6.

<sup>17</sup> Ibid., 459.

<sup>2</sup> Jour. Amer. Med. Assoc., January, 1908.

<sup>4</sup> Berl. klin. Woch., July 6, 1908.

<sup>6</sup> Virchow's Archiv, June, 1907.

<sup>11</sup> Brit. Med. Jour., December 31, 1904.

<sup>13</sup> Quoted by Robinson, loc. cit.

<sup>15</sup> Arch. Int. Med., October, 1908.

<sup>17</sup> Lancet, November 10, 1906.



so close, indeed, that it is sometimes difficult to demonstrate any dividing connective tissue, it is possible that in cases of long-standing heart-block some of the muscular fibers outside of the bundle might assume a compensatory function and conduct the stimulus from the auricle to the ventricle. This does not seem to be a satisfactory explanation, since the fibers of the bundle normally seem to be highly specialized and quite different in appearance from the ordinary cardiac muscle tissue. Furthermore, Erlanger's<sup>21</sup> recent researches seem to show that functional union cannot be reestablished between two parts of the heart the functional continuity of which has been completely severed. But, on the other hand, we must bear in mind that we have still much to learn regarding not only the physiology, but even the anatomy of the auriculo-ventricular bundle. Thus, only recently Curran<sup>22</sup> has found in human, in calves', and in sheep's hearts a bursa which is in constant relation to the bundle, which would facilitate the extension of infection from the endocardium, and which, in the event of a bursitis, might greatly impair its function. The mere existence of the bursa would seem to indicate that either the bundle did not contract at all or that it contracted differently from the rest of the heart muscle. If the lesion had been a gummatous one, it is conceivable that antisyphilitic treatment might have restored the function of the bundle, but in the present case lues could be excluded, the administration of iodide was useless, and the patient did not recover during or even soon after its employment. (Recoveries as the result of antisyphilitic treatment have been reported by Schmaltz<sup>23</sup> and Erlanger.<sup>24</sup>) Some investigators believe that conduction through the bundle is nervous in character and not muscular at all. This view is not generally accepted, although the supporters of the myogenic hypothesis readily admit that stimulation of the vagus nerve depresses the function of conductivity. (This has been shown by Gaskell,<sup>25</sup> and by Mackenzie.<sup>26</sup> Furthermore, digitalis, which acts upon the heart mainly through depression of the vagus, is known to depress this function in cases in which it is already below par, thus producing digitalis heart-block.) Then again a vagus block would have been more likely to be incomplete, and intermittent. If the heart-block in the present case had been the result of overaction of the vagus it would have disappeared or at least shown some improvement under the large doses of atropine which were administered, whereas it remained absolutely unaffected, except for one temporary rise in pulse rate, even while the full physiological effects of the drug were manifested throughout the rest of the system.

<sup>21</sup> Amer. Jour. Physiol., July, 1909.

<sup>22</sup> Münch. med. Woch., 1905, p. 1120.

<sup>23</sup> Text-book of Physiology, edited by Schaefer, vol. ii.

<sup>24</sup> Manchester Med. Chronicle, September, 1906.

<sup>25</sup> Anatom. Anzeiger, 1909, xxxv, 89.

<sup>26</sup> Jour. Exper. Med., 1906.

Wiesel<sup>27</sup> has described three cases of coronary sclerosis, with symptoms of angina pectoris, in which there was extensive fibrosis of the bundle both above and below its bifurcation, in which none of the symptoms of the Adams-Stokes syndrome had occurred. In such cases, however, it is often difficult to be sure that all of the fibers have been destroyed, and that the functionation may not have been due to a few healthy fibers.

Transient heart-block sometimes occurs during or shortly after an attack of infectious disease, and in such cases is evidently the result of a toxemia<sup>28</sup> or inflammation.<sup>29</sup> No such explanation could be applicable to the present case.

Belski<sup>30</sup> has reported a case of heart-block in which a temporary restoration of conductivity was noted, although the *a-c* interval remained prolonged throughout, and a slight exertion, such as sitting up in bed, would again bring on the block. Among the three cases recorded by Gerhardt, in which a heart-block disappeared after existing for some time, there was one which had some similarity to the present case. The patient was a woman, aged sixty-five years, in whom complete block alternated for several days with normal auriculoventricular coördination, and finally disappeared altogether. The patient was the subject of arteriosclerosis, a process in which the auriculoventricular bundle probably shared. This second of Gerhardt's cases is the only one which I have been able to find in the literature which resembled Dr. Earnshaw's case, and this one was of much shorter duration and of less intensity.

Herrick<sup>31</sup> recently has reported a case presenting some points of similarity to that herewith reported. Although Herrick's patient seems to have made a symptomatic recovery, the phlebogram discloses a permanent depression of conductivity.

From a study of the hitherto reported cases of the Adams-Stokes syndrome, both those with and without autopsy reports, it would seem that the auriculoventricular bundle may be more or less destroyed by pathological processes without giving rise to dissociation. So long as there are some healthy fibers left, they seem to be capable of conducting contractile impulses. It also seems to be shown, that these remaining fibers may temporarily lose, and subsequently regain, their function as the result of a number of factors, such as drugs, toxemias, inflammation. It is reasonable to suppose that when a transient heart-block occurs in a patient of advanced years there is some organic, probably arteriosclerotic, change in the bundle; and that the block occurs by virtue of some superadded factor which has deranged its nutrition.

<sup>27</sup> Kongr. f. inn. Med., 1907, p. 628.

<sup>28</sup> Joachim, Deut. Arch. f. klin. Med., 1907, lxxxviii, 4 to 6.

<sup>29</sup> Gerhardt, Ibid., 1908, xciii, 5 and 6.

<sup>30</sup> Zeit. f. klin. Med., vol. lvii.

<sup>31</sup> AMER. JOUR. MED. SCI., 1909, cxxxix, 246.

The most reasonable explanation which we have been able to formulate in explanation of the present case has been a vasomotor one, probably engrafted upon some sclerotic change in the bundle or its nutrient vessels. The auriculoventricular bundle is, of course, nourished by definite branches of the coronary artery. Vascular sclerosis is often curiously localized in distribution. Thus, in the field of medicine which we have been considering Karcher and Schaffner found the bundle well preserved in a case of high-grade coronary sclerosis, and Aschoff describes well-marked arterial disease affecting the small arteries which supply the bundle, and yet the bundle itself was in an apparently healthy condition. It is conceivable that if for some reason the blood supply of the bundle was temporarily cut off or diminished, it would cease functioning as long as the anemia kept up, and again take on its normal activity when its blood supply was reestablished. That there may have been some such diminution of blood supply resulting from round-cell infiltration, arterial spasm, or constriction, or alteration in local blood pressure, would be nearly as difficult to deny as it would be to prove. At all events, this seems to be the most rational explanation which can be offered to explain the case in question.

I wish to express my indebtedness to Drs. Norris, Stengel, Pepper, and Thayer for their assistance in the study of the case.

## A CLINICAL STUDY OF TWO CASES OF CARDIAC DEATH.

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MUCH remains to be determined regarding the causes of cardiac complications arising during the course of, or following, the acute infectious diseases. A great deal of light is being thrown upon this subject by the experimental studies of Pearce,<sup>1</sup> Fisher,<sup>2</sup> Welsh and Flexner,<sup>3</sup> Bolton and Bown,<sup>4</sup> Fleischer and Loeb,<sup>5</sup> and Sharp.<sup>6</sup> Postmortem investigations in the infectious diseases have demon-

<sup>1</sup> A note on the Production of Vascular Lesions in the Rabbit by Single Injections of Adrenalin, Albany Med. Annals, xxviii, 51.

<sup>2</sup> Ueber Arterienkrankungen durch Adrenalin Injectionen, Münch. med. Woch., 1905, iii, 928.

<sup>3</sup> Histological Changes in Experimental Diphtheria, Bulletin Johns Hopkins Hospital, 1891; The Histological Changes Produced by the Toxalbumin of Diphtheria, *ibid.*, 1892, iii, 17.

<sup>4</sup> Pathological Changes in Central Nervous System in Experimental Diphtheria, *Brain*, xxx, 365.

<sup>5</sup> Archives Int. Med., iii, 78.

<sup>6</sup> Jour. Anat. and Phys., 1897, xxxi, 199.

strated profound changes in the heart muscle, as the result of the action of the various microbiotic poisons. These conditions are analogous with changes occurring in the skeletal muscles in like disorders. The first studies upon the condition of the heart muscle in infections were made in a case of typhoid fever, but the most minute observations have been carried on in regard to diphtheria. In diphtheria, in addition to myocardial changes, there has been demonstrated degeneration of the medullary centres, of the peripheral vagus, and of the cardiac plexus (Vincent and P. Meyer). Romberg and Paessler have pointed out that the circulatory disturbances which arise in animals infected with pneumococcus, *Bacillus diphtheriæ*, and *Bacillus pyocyaneus* are caused almost exclusively by central paralysis of the vasomotor apparatus.

In applying observations made on pneumococcic septicemia in animals to human beings afflicted with pneumonia, it must be remembered that in pneumonia the condition is not quite analogous, since in this an additional strain is thrown on the heart by reason of obstruction in the pulmonary circuit. Krehl<sup>7</sup> concludes his discussion of the subject of cardiac involvement in diphtheria by saying that all that we can state definitely at present regarding the subject, is that the diphtheria poison injures the heart muscle and the vasomotor apparatus. It is probable that in the near future further studies in experimental myocarditis, induced by the injection of adrenalin or by inoculation with toxins, will throw additional light upon the matter.

The interest of this subject lies not alone in the field of the experimental physiologist and of the pathologist. The clinician must add his observations as to the effect which these poisons produce upon the living as demonstrable at the bedside. The symptoms of cardiac involvement are not infrequently somewhat obscure; yet, if such signs as are present be disregarded, there may occur an unexpected and perhaps an avoidable death, which, by careful examination, could have been at least foreseen.

CASE I.—M. J., a female, aged six years, a well-nourished child, with no history of previous severe illness. She was first seen October 5, 1906, when she was found to have typical tonsillar diphtheria. Diphtheria bacilli were subsequently demonstrated in pure culture. On the following day the exudate had spread to the pharynx. There was moderate toxemia. The urine was normal. The heart sounds were markedly clear, and the pulse regular and full. The fever was not at any time high. Antitoxin was administered on this and on the succeeding day—6500 units in all—after which the child began to improve, and by October 10 she was practically well; the exudate had disappeared; the temperature had fallen to normal; the general condition was so good that

<sup>7</sup> Diseases of the Heart, Nothnagel's Encyclopedia, 635.

the parents regarded the little patient as well. As yet there was no circulatory change demonstrable.

On October 11, in the evening, the child complained of feeling chilly, but did not have a true rigor. She had been particularly cheerful all day. The evening was cool; so she was wrapped in a blanket and was soon quite comfortable. On October 12 she had a sudden attack of severe epigastric pain with vomiting; these symptoms continuing throughout the day. There had been no indiscretion in diet and her bowels had been moving freely. A physical examination showed that the heart sounds had become muffled, and it was noticed that the radial pulse was markedly arrhythmic. The child's face was pale and anxious, and the skin surface was decidedly cool. The examination of the abdomen showed epigastric tenderness, but was otherwise negative. The family was warned of the danger, and instructed to keep the patient absolutely quiet upon her back, to have some one person with her constantly, and to avoid all excitement. The use of the bed pan was insisted upon. The further course of the case was as follows:

On October 13 vomiting and pain were still present, but they were of a less severe nature; the pulse was very weak and intermittent; the heart impulse was weak, the muscular sound poor, but no murmur was audible.

On October 14 improvement continued; there was no pain; there was occasional slight vomiting, but nourishment was retained fairly well; the bowels moved; the pulse was of better quality. In the evening the child was left alone for a short time by the member of the family who was acting as nurse. The patient called, and, receiving no answer, became much excited, screamed violently and repeatedly, and, when the nurse returned, was so nervous that "she shook all over," and could not be quieted for a long time.

On October 15, when she was seen about midday, the condition was fairly good; she had slept the greater part of the night, the pulse was somewhat better in quality than it had been previously; but the heart sounds were muffled, and the beat irregular as to rhythm and force; no murmur was heard. One hour later I was called hurriedly and found her in collapse. Her nurse, on being questioned, said that at about 12.30 the child had called out that she was about to have a movement of the bowels. The bed pan was brought, but she became greatly excited and insisted on being allowed to sit up. This the nurse (a sister) finally allowed her to do, although she had been fully warned against the danger of such proceeding. Almost immediately the little patient gave a long sigh, her arms dropped to her sides, she became deathly pale, and could return no answer to the frenzied questions put to her. She died at 4.30 P.M., never having reacted nor regained consciousness.

The case appears to be a typical one of cardiac death occurring in convalescence from diphtheria. Only a few points of interest will be considered in regard to it.

*Time of Appearance of the Cardiac Symptoms.* Two forms exist, an early and a late. Heart failure in the acute stage is seen only in the severest forms of infection. It may occur without warning, or there may be prodromal signs of failure of the circulation. Death in convalescence may be sudden, but is more frequently preceded by signs and symptoms of abnormality of heart action. "But the most curious thing is that, for a long time, weeks after the disease itself has run its course, and when the patient is convalescent there is still danger of the occurrence of severe circulatory disturbances" (Krehl<sup>8</sup>).

*Danger Signs.* Vomiting is, as a rule, an indication of the beginning of degeneration of the vagus nerve. "There is no one symptom in the convalescent stage of diphtheria which is of so grave import as a sudden unexplained attack of vomiting. Very few patients in this condition recover" (McCollum<sup>9</sup>). Other serious symptoms are marked pallor, coming on perhaps suddenly, and abdominal pain and tenderness. Among the dangerous cardiac symptoms are an increase in frequency, or a marked slowing of the heart beat. Irregularity of force and rhythm, with a muffling of the muscular sounds are always to be taken seriously as of bad prognostic omen. The association of gallop rhythm with late vomiting renders the outlook almost hopeless (White and Smith<sup>10</sup>).

*Frequency.* Romberg and Schmaltz claim that circulatory disturbances occur in 10 to 20 per cent. of all cases of diphtheria.

*Effect of Antitoxin.* Authorities disagree. Krehl<sup>11</sup> says that as far as can be judged, serum treatment has no appreciable influence upon the frequency of circulatory disturbances. White and Smith<sup>12</sup> conclude that antitoxin does not affect the heart, unfavorably, but that, on the other hand, its early use prevents the appearance of grave heart complications. Rosenau and Anderson<sup>13</sup> have reported the remarkable prophylactic effect of the early use of antitoxin against postdiphtheritic paralyses in guinea-pigs.

*Treatment.* When severe heart complications have developed, absolute rest in bed and absolute avoidance of excitement, perhaps for weeks, are necessary. One may, however, be governed somewhat by the stage of the illness and the general condition. If no serious trouble has developed within four weeks the patients are, as a rule, safe from this complication (White and Smith). They are not, however, entirely out of danger.

*Action of the Toxins and Microorganisms upon the Circulatory Apparatus.* The infection is frequently mixed—a fact which complicates the problem. Baginsky<sup>14</sup> says: "If we ask ourselves what anatomical change the heart muscle in these conditions and

<sup>8</sup> Loc. cit.

<sup>10</sup> Communications of Mass. Med. Soc., 1904. Quoted by McCollum, loc. cit.

<sup>11</sup> Loc. cit., 637.

<sup>12</sup> Trans. Assoc. Amer. Phys., xxii, 26.

<sup>9</sup> Modern Medicine, ii, 416.

<sup>13</sup> Loc. cit.

<sup>14</sup> Mod. Clin. Med., p. 516.

processes has suffered we would be greatly mistaken if we assumed that they are always very marked or constantly of the same nature. Occasionally, in fact, nothing is found which could at all explain the loss in the action of the heart; and this is especially the case if death has occurred quite rapidly. In these cases, probably, lesions of the cardiac nerves and ganglia arise which can only be demonstrated with the greatest difficulty. On the other hand, however, there is found, especially in those cases in which the agony has lasted some time, and in which the improved conditions have varied with renewed collapse, the grossest changes in the heart muscle; fatty degeneration of the muscular structure, gross changes in the nuclei of the muscles, and complete fragmentation or hemorrhagic dissemination of the muscular tissue, and with this adhering thrombi which have most probably occurred during life."

The theory of Eppinger is accepted by Trumpp<sup>15</sup>—that of a separation of the fibrils of the heart muscle from their sheaths—a myolysis from toxic oedema. Adami<sup>16</sup> regards vagus degeneration as the most satisfactory explanation of the sudden deaths which occur in diphtheria. His is a view to which I incline, as best explaining the terrible sequel of this case.

CASE II.—Miss P. Y., aged fifty-four years. She had been a healthy child up to her ninth year, at which time she had an attack of scarlet fever, moderate in its severity. There were apparently no complications, and she was subsequently in good health until three years later, when she passed through a severe attack of diphtheria. She was confined to her bed for four months. The cause of this protracted illness is unknown, but the family states definitely that there were no paralyses. A short time after she was able to be on her feet again, she began to suffer from severe attacks of asthma, usually lasting for three or four days. During the intermissions, of several weeks' duration, she was entirely free from respiratory disorder. She never, however, regained her previous bodily strength.

When twenty years of age she began, for the first time, to complain of palpitation during her asthmatic attacks, although she continued free of cardiac symptoms during the intermissions. Following a change of dwelling to a somewhat higher altitude, the attacks of asthma and palpitation greatly diminished as to frequency, and she had comparative freedom for nearly twelve years, when the symptoms of cardiac insufficiency began to return, and to assume the major role. She still had attacks of asthma and suffered from bronchitis and emphysema; but the heart was evidently somewhat crippled at this time, for she was very short of breath on exertion, and oedema set in. There were frequent attacks of tachycardia, and the family later began to notice a dusky color about her lips and

<sup>15</sup> *Diseases of Children*, Pfandler and Schlossman, ii, 386.

<sup>16</sup> *Principles of Pathology*, p. 433.

fingers. Her asthmatic attacks were comparatively infrequent from this time on, but the cyanosis became so marked that a sister described her as having times when her hands would be "black to the knuckles." The latter condition set in about two years before her death, and had no relation with her attacks of dyspnoea. During the last few months there were "two occasions when the forehead and cheeks became almost black." She complained of dyspeptic symptoms and of pain in the right hypochondrium. During the two months before her death, her sister noticed a throbbing of the veins in her neck—this an independent observation and not the result of a leading question. The skin was always sallow. She began to be apathetic, but in spite of her discomfort was able to attend to light duties about the house.

I was called to see her on March 6, 1909, and found her walking about her room in great respiratory distress. Her face and finger nails were livid, the general surface dusky, and the conjunctivæ icteric. She was troubled with frequent cough, and was expectorating a viscid, blood-stained mucus. Physical examination revealed a general arteriosclerosis, a radial pulse of marked irregularity and weakness, throbbing jugulars (ventricular venous pulse), an apex beat diffuse in the fifth and sixth interspaces somewhat within the nipple line. The transverse area of cardiac dulness extended from three and one-half finger breadths to the right of the sternum, to the left nipple line. The lungs showed evidence of chronic bronchitis. There were also many piping asthmatic rales. There was an area of beginning consolidation at the right base posteriorly. Examination of the heart showed a tumultuous irregular action, the muscle sound very poor—apparently a soft, systolic murmur at the apex and over the lower portion of the sternum. It was difficult to be certain of this, as the conditions for examination were exceedingly unfavorable. There were very poor aortic and pulmonary second sounds. The liver extended to the level of the umbilicus, was tender to the touch; no pulsation could be detected. An extremely unfavorable prognosis was given owing to the patient's age and to the condition of the heart. Her family was warned of the danger of sudden death.

When she was seen next morning the patient's mind was relatively clear. The temperature was 102°. There was little evidence of toxæmia. The heart conditions had remained apparently unchanged. The consolidation at the right base had increased in area, and a beginning involvement of left base was apparent. A few hours afterward the very competent nurse in attendance took the patient's pulse and found it unchanged. She stepped into the hall and was absent, she says, but a minute. When she returned she was shocked to see the patient evidently in a dying condition. In a minute or so breathing had ceased.

I will not attempt to discuss this case in detail, but only in rela-



tion to the cardiac complication. As the patient was not seen until near the termination of her case, and as any conclusions which are drawn must rest upon the history and upon the untrained observations of members of her family up to the appearance of her terminal pneumonia, a complete diagnosis of her condition was beset with many, perhaps insuperable, difficulties. Further, the presence of her pneumonia and of her excessively weak heart, masked certain symptoms and made perhaps of doubtful import such others, as the enlargement of the liver, the jaundice, the cyanosis, and the increase of cardiac dulness to the right which was present at the time of examination. A point which, from a study of her history, strikes me at the very beginning, is the comparatively late period at which symptoms of a failing circulation began to develop—that is, the amount of work which a weak heart may be able to perform.

That the original cause of weakness of the heart muscle may be traced to the diphtheria forty years before seems not impossible. We have noted that at that time the patient had been confined to her bed for four months. It is stated quite definitely by an intelligent member of the family that there were present no paralyses to account for this long illness. The known frequency of myocardial complications in the disease under consideration makes it, therefore, not unlikely that to a damaged heart muscle must be attached the blame of this protracted convalescence. The duration of the illness corresponds with the course of myocarditis of convalescents, some cases of which are often protracted for weeks, or even months.

The important point to be considered is, whether a myocarditis arising in childhood could affect the heart during so long a period as forty-two years. As bearing upon this point I quote from Krehl:<sup>17</sup> “The *restitutio ad integrum* in many cases of diphtheritic heart disease that end in recovery is so complete that an ordinary physical examination reveals nothing whatever. But it is a question, nevertheless, whether the heart is really absolutely sound, especially whether it has the same functional capacity as before, or, in other words, whether its capacity is adequate to the demands incident to the individual's mode of life. The more we study heart diseases the more we are impressed with the extreme complexity of the etiology; an infectious disease that has run its course many years before a definite disease of the heart develops, appears, nevertheless, to be capable of influencing the development of this disease, although the interval between the two events may have been marked by perfect health. Possibly the first disease prepared the soil for the second.”

We note that for eight years after her diphtheria the patient had no cardiac symptoms, or, at least, none that were observed. During this time, she was greatly troubled by attacks of asthma, the pre-

<sup>17</sup> Loc. cit., 638.

disposition to which disease may have arisen through catarrhal conditions of the respiratory mucous membrane resulting from her diphtheritic infection. It is possible that the cardiac affection was responsible. The long period of asthma without apparent cardiac inadequacy, and the fact that the asthma diminished as the heart became less and less able to carry on its work, suggest, however, that some exciting cause was present outside of the myocardium. It may be noted as a matter of interest that McPhedran<sup>18</sup> claims that true asthma is very rarely due to diseases of the heart. Jellenk and Cooper<sup>19</sup> suggest that cardiac asthma may arise in certain instances as a right-sided angina. Whether we consider the asthma of cardiac origin or not, it is certainly of interest that, for over a period of many years, circulatory disturbances played only a secondary role in the clinical picture, and that it was not until the later years of her life that symptoms of cardiac incompetence became of overshadowing importance. A longitudinal section of her history shows us, then: a period of eight years of asthma without circulatory disturbances; thirty-two years of asthma with coincident cardiac distress but freedom between attacks; and a later period during which the asthmatic attacks became less frequent while the trouble with the heart increased. We have learned that it was only during the last two years of her life that marked cyanosis became noticeable to the untrained members of her family, but that the marked pulsation of the veins of her neck were visible for two months before her death.

What had happened to the heart during this period? To an organ which we have assumed to have been early weakened by a toxic myocarditis and later to have participated in a general condition of malnutrition, which we have seen existed since her twelfth year, has been added a frequently recurring strain. The cardiac strain in asthma falls particularly upon the right heart, and in the patient under consideration the throbbing veins of the neck and the attacks of extreme cyanosis with subicteric color of the skin and conjunctivæ, noted by the family, give support to the view that during the later period there was a gradually increasing dilatation of the right ventricle with resulting incompetence of the tricuspid valves. The marked congestion of the liver observed at the time of examination and the history of right hypogastric pain give some further support to this view.

Further cause of dilatation of the right heart may have existed in an insufficiency of the mitral valve. Clinical proof of such condition is wanting; but, when we remember how often a muscular insufficiency of the mitral valve exists, even in a pure myocarditis, and when we further consider the frequency with which myocarditis and true endocarditis co-exist, it would certainly have been quite

<sup>18</sup> Modern Medicine, iii, 712.

<sup>19</sup> Amer. Med. Jour., vol. 1, No. 9.

within ordinary experience to have had such cause of pulmonary engorgement present in this case. That no mitral murmur was heard at the time that the patient came under observation could not, of course, exclude such condition.

Finally, a persistent low blood pressure may have been an additional cause of weakness of the heart muscle as a whole. How much, if any, of this was due to vasomotor influences and to a massing of blood in the splanchnics cannot be determined. We can only say that at the beginning of the patient's pneumonia she had a very low arterial pressure, and that it is not unlikely that such a condition had been present for some time. Here, then, we would have a possible establishment of a vicious circle, for, as soon as the left ventricle can no longer maintain a sufficient degree of pressure in the aorta to maintain the requisite pressure in the coronary artery, the myocardium suffers from hyponutrition at the very time when it can least afford to dispense with its proper supply (Hoover<sup>20</sup>).

Then as a last straw comes pneumonia, with a toxin in the circulation capable of further damaging the heart muscle, and an added work is thrown upon the already weakened right ventricle by reason of the obstruction in the pulmonary circuit. That the heart could not respond to this additional call is shown by the weakness of the pulmonic sound throughout.

I have spoken of dilatation of the right ventricle resulting in failure at closure of the tricuspid valves—a relative incompetence which is almost the only form seen developing in adult life, except in connection with previously existing valvular disease involving other valves of the heart. The mechanism of this functional incompetence is, that as the dilating right ventricle expands, the fibrous ring surrounding the auriculoventricular orifice becomes stretched. A larger opening is thus formed, and as the chordæ tendinæ cannot elongate, the cusps can no longer meet in close apposition. Further, "It is a question whether the inability of the muscle to lessen the ventricular cavity to its normal size in systole does not play a large, if not the chief part, for if at the height of systole the cavity were no larger (than normal), it is conceivable that even with a dilated ring no regurgitation might occur; but if with a dilated ventricle the degree to which the ventricle can contract be lessened, then the cavity is fuller at the end of systole than normal, and the valve cusps are not properly approximated" (Osler<sup>21</sup>).

SUMMARY. It may, therefore, be concluded with a fair degree of certainty that the cause of death was incompetence of a heart muscle, probably the seat of a chronic myocarditis. This condition may have originated at the time of the infection with diphtheria during childhood, or, at least, the soil may have been prepared at that time for subsequent cardiac disease. That the scarlatinal infection may have

<sup>20</sup> Modern Medicine, iv, 31.

<sup>21</sup> *Ibid.*, 240.

exerted some unfavorable influence cannot, of course, be denied. At any rate, owing to repeated strain and to various unfavorable conditions there gradually developed the incompetence of the muscle for the work required of it. Dilatation of the right ventricle set in, with relative insufficiency of the tricuspid valves; the fatal end was precipitated by a sudden increase in resistance in the pulmonary circuit, with possibly a further weakening of the muscle as a result of the action of the toxic products of a pneumococcic infection.

It is regretted that autopsies could not be obtained in either of the above cases; but, since the wide field of speculation into which a bedside study of certain heart cases may lead us opens up many subjects which even a careful postmortem examination might fail to make wholly clear, their report seems, nevertheless, justifiable.

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### INFLUENZAL SEPTICEMIA.

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THE invasion of the deep tissues and the blood by the influenza bacillus has been a matter of much doubt, and up to recent times has received but little bacteriological confirmation. That it does more or less frequently invade the blood stream can no longer be doubted. When we consider the accumulating evidence of the comparative frequency among severe influenzal infections, of such complications as endocarditis, arteritis, phlebitis, arthritis, etc., we must be impressed, I think, with the probable frequency with which this organism finds its way into the blood and there succeeds in living and multiplying. Doubtless a simple transmission by the blood to other parts, without the organism actually growing in the blood, may occur.

One striking feature noted in connection with certain cases of the grip is the marked prolongation of the fever, suggesting the continued operation of the organism in the tissues rather than a mere delay in the recovery from an infection lasting only a few days. In many of these prolonged attacks there has been no bacteriological evidence forthcoming to prove what organ formed the nidus of the bacillus. However, in not a few there has been demonstrated a definite complication, such as otitis media, pleurisy, pneumonia, pericarditis meningitis, arthritis, etc., and from these has been isolated the influenza bacillus. There are still other cases of prolonged fever in which none of these complications appear, or at least play a minor

part, and some of these have been shown to be true influenzal septicemia. These are the cases which resemble closely typhoid fever or other infections such as miliary tuberculosis. That these cases have been long wanting an explanation we can readily understand when we consider the comparative difficulties in the way of obtaining these organisms in cultures.

The following case represents a prolonged influenzal infection in which there was a primary bronchopneumonia followed by invasion of the blood and ending in recovery.

V. A., a female, aged thirty-eight years, married; the family history is unimportant. She never had typhoid fever, nor had she been troubled with a chronic cough. During the latter months of her only pregnancy she suffered from a "milk leg" on the left side, from which she recovered completely. The present illness began December 12, 1906, while on the train going to a nearby town. She became chilly, felt badly all over, experienced a sort of numb sensation, and was nauseated and vomited. On reaching her destination she found it necessary to go to bed. A physician was called, and found her with a high fever and severe pains all over the body, and spoke of her having rheumatic fever. On December 18 she returned to Milwaukee, and when seen by a physician had a temperature of  $103.8^{\circ}$ , complained of extreme general malaise, and looked very ill. There was some cough and a little expectoration, no diarrhoea, but at first some pain over the lower abdomen. The patient was seen with Dr. McNaughton on December 21. She then seemed feeble and very ill. There was some cough, and she was expectorating a moderate amount of brownish or bloody sputum. She complained of a sharp pain in the right side on coughing or taking a deep breath. There was no abdominal pain and no diarrhea.

The patient was a small, frail woman. The chest was poorly formed and bony. On the left side nothing abnormal was found beyond an occasional rale. On the right side expansion was slightly lessened, but the percussion note and vocal fremitus seemed nowhere distinctly abnormal. Over the front, at the apex, and especially at the level of the third and fourth ribs, many crackling rales were heard, some quite coarse. In the right axilla a well-defined friction rub with some fine crackles was heard. Behind and especially in the lower interscapular region a good many rather coarse rales were noted. No tubular breathing or exaggerated voice sounds were anywhere present, though the breath sounds were relatively suppressed. The abdomen was flat, not tender, and there were no rose spots. The spleen was not palpable, but the area of splenic dulness was somewhat increased. The leukocyte count was 7500 and the Widal test negative. The sputum was moderate in amount, tenacious, and at first distinctly brownish and blood-stained. During the following month the patient's general condition showed no improvement, though the lung symptoms had very distinctly abated.

The cough and expectoration gradually lessened and practically disappeared. The friction rub on the right side had disappeared, and nearly all the rales were gone. There was still some deficiency of breath sounds on the right side. The spleen remained about as noted and no rose spots were seen at any time. She continued to have fever which, however, it was not possible to observe as accurately as was desirable. During this time the temperature was quite irregular, rarely touched normal, often rose to  $102^{\circ}$  to  $103^{\circ}$ , and for the most part showed an afternoon rise. There were periods when, on the whole, the fever showed abatements. Its total duration was about sixty-eight days.

On January 21 some pain was complained of in the right groin, and on the next day the region below Poupart's ligament was tender and rather diffusely swollen. In the region of the femoral vein a painful induration 10 cm. long could be made out. The femoral artery at this point could be felt pulsating, as also could the post-tibial and dorsalis pedis. The whole limb was slightly swollen, but it was most marked about the foot and ankle. At the end of a week the pain and swelling had somewhat lessened. At 7 A.M. January 29, the patient experienced a chill which lasted some minutes. The next morning, and again at 6.30 P.M., there was a severe chill, each being followed by a high fever. During this period the fever was particularly irregular, ranging between  $98^{\circ}$  and  $106^{\circ}$ . On February 3, an arthritis developed in the left wrist. The wrist became red, swollen, and painful. This condition increased in intensity and the patient complained of much pain. A considerable boggy swelling developed, but on aspiration no fluid could be obtained. The patient was moved to the Milwaukee Hospital on February 16. At this time her general condition had distinctly improved; the temperature was ranging between  $98^{\circ}$  and  $100^{\circ}$ . The right leg was still distinctly swollen, the induration was readily made out in the groin, and could be distinctly traced to the popliteal space, where there was induration, pain, and tenderness. The left wrist was now much better, though there was still distinct swelling on the dorsum and limitation of motion.

During the following month both the wrist and the leg improved slowly but continuously, and at the end of six to eight months both conditions were entirely well. There was no fever after February 17. The cough had entirely disappeared, the condition of the chest was about normal, and when examined two years later, the lungs and the heart were normal, as also were the right leg and left wrist. The Widal test taken on subsequent occasions was negative for both typhoid and paracolon bacilli. The urine examinations showed nothing abnormal of importance beyond a trace of albumin.

Smears from the sputum stained by Gram's method and counter-stained with Bismarck brown showed a variety of organisms, the vast

majority of which were a small non-Gram staining bacillus having the morphology of the influenza bacillus. Cultures from the sputum were made on blood agar in the usual way and the influenza bacillus was quite readily grown and isolated in pure culture. A good many other organisms grew and among them were colonies of pneumococci, but the scarcely visible colonies of the influenza bacillus vastly predominated. Repeated examinations were made for tubercle bacilli, but none was found. On February 2, about an ounce of blood was obtained from one of the large veins of the arm. Portions of this were transferred to three blood agar tubes and a bouillon tube; at the end of thirty-six hours the cultures in the agar tubes showed many colonies just visible in a proper light and under a lens, resembling very much small drops of dew. No other colonies were present. A growth of influenza bacilli was also obtained in the bouillon. On being transferred to other blood agar tubes a faint growth was again obtained, but on plain agar no growth appeared after several days in the thermostat. A smear from these fine colonies showed a small non-Gram staining bacillus resembling accurately those obtained in culture from the sputum. Because of the objections of the patient no further cultures from the blood were made.

Many observers have described influenza bacilli in the blood from the earliest time of our knowledge in regard to this organism. In fact, in the same publication which contained Pfeiffer's preliminary communication, Canon<sup>1</sup> claimed to have found the influenza bacillus in the blood in nearly all of 20 cases of acute influenza. These organisms were found microscopically, but were not obtained in cultures. Klein<sup>2</sup> also at this time found the organism in the blood, but much less frequently: only six times among 43 fresh cases. Pfuhl<sup>3</sup> and others also obtained positive results microscopically, and most of the other observations in the literature at this time were demonstrated in this way.

On the other hand, Pfeiffer and Beck<sup>4</sup> took decided exception to this, and claimed never to have found the organism in the blood either microscopically or culturally, though Pfeiffer admits seeing the influenza bacillus twice in microscopic sections and several times growing a few colonies from the spleen and kidney. Not a few observers have found the organism in the blood microscopically, but failed in their attempt to grow it. It is probable that not infrequently dead organisms are present in the blood.

At autopsy the influenza bacillus has been obtained in cultures from the heart's blood by Jehle,<sup>5</sup> Rosenthal,<sup>6</sup> and Doering.<sup>7</sup> Jehle's observations are most interesting and important. His cultures were

<sup>1</sup> Deut. med. Woch., 1892, xviii, 28.

<sup>2</sup> Centralbl. f. Bacteriol., etc., 1892, No. 13, p. 397.

<sup>3</sup> Ztschr. f. Heilkunde, 1901, xxii, 3 abth., p. 190.

<sup>7</sup> Münch. med. Woch., 1900. xlvii, 1530.

<sup>2</sup> Brit. Med. Jour., 1892, i, 170.

<sup>4</sup> Deut. med. Woch., 1892, No. 21.

<sup>6</sup> Thèse, Paris, 1900.

all made at autopsy. The influenza bacillus was most commonly found in the blood of patients dead of the acute exanthematous diseases. The blood of 48 cases of scarlet fever was examined culturally and the bacillus isolated in 22 cases. In 19 cases a pulmonary influenzal infection was present. In 15 of these the blood was positive for the influenza bacillus, while in only 4 cases was it negative. In the other 7 cases in which bacilli were found in the blood no influenzal infection of the respiratory tract could be established, though in three cases these organisms were demonstrated in the parenchyma of the tonsils, and in these cases he regards the tonsils as the probable portal of entry. The bacillus was not always found in the blood in pure culture, as in four cases they were associated with streptococci in varying numbers. In one case, with numerous bacilli in the bronchial secretions, only staphylococci were found in the blood.

Among 23 blood examinations of patients dead of measles the influenza bacillus was found 15 times. In 18 cases the measles was complicated by pulmonary influenza, 9 of which were bronchopneumonia; and in 13 of these the organism was found in the blood. In 2 cases showing influenza bacilli in the blood, no bacilli could be demonstrated in the respiratory tract. One of these cases showed a large number of bacilli in the tonsils.

In 9 cases of varicella with influenzal involvement of the lungs, 5 showed influenza bacilli in the blood. In 24 cases of whooping cough the blood was examined, but in only 2 cases were the bacilli found, though in the bronchial secretions they were obtained in every case in greater or less numbers. Fifteen cases of diphtheria were examined, in 9 of which there was an influenzal infection of the respiratory tract. In only one of these cases were influenza bacilli found in the blood. A group of 20 cases suffering from a variety of diseases, but all showing pulmonary influenza, was studied; among these, in only 3 cases could the bacillus be demonstrated in the blood. In one case, which was clinically considered to be a case of pyemia, there came in addition a severe angina, a double pleurisy, and a fibrinous pericarditis. At autopsy great numbers of influenza bacilli were found in the pleural and pericardial exudates, and also a few unidentified diplococci. The two other cases occurred in connection with severe endocarditis. In both cases there was an ulcerative condition of the heart valves. Bacteriologically, in the one, there were very many influenzal bacilli in pure culture, in the other, there were also a great many bacilli, but associated with a few diplococci. Thus, Jehle isolated the influenza bacillus from the blood in 48 cases; 42 of these cases were among the acute exanthematous diseases, while there were only six among other diseases with influenza of the respiratory tract. Especially with scarlet fever and measles, the results would seem to indicate that the bacillus readily finds its way into the blood, and this may happen in the early stages even before



the rash has appeared. On the other hand, among other diseases with respiratory influenza it appears to be not nearly so common.

Thus far we have dealt only with cases in which the influenza bacilli were found in the blood at autopsy or were insufficiently demonstrated during life. Metnier<sup>8</sup> was among the very first to actually demonstrate their presence in the living blood. He reports ten cases of influenzal bronchopneumonia complicating measles, in eight of which cultures were made from the blood and in four instances bacilli in pure cultures were grown, the other four being sterile. The cultures were made from ten days to a few hours before death, all of the four cases proving fatal. In a note he has added one more case of influenzal bronchopneumonia in which he grew the bacillus from the blood, thus making five in all. He does not state whether or not this case resulted fatally. In all of the cases other organisms in varying numbers, such as the staphylococcus, streptococcus, or pneumococcus were found in the pulmonary secretions, although in the majority of them a pulmonary puncture brought forth a pure culture of influenza bacilli, and in others this organism vastly predominated. In these cases of pneumonia he accords to the influenza bacillus the principal role.

Horder<sup>9</sup> reports two cases of influenzal septicemia in which he obtained the bacillus in pure culture from the blood, four times in one case and twice in the other. In one case the cultures were obtained six weeks, and in the other case five weeks before death. Both were cases of malignant endocarditis thought to be engrafted upon an old endocardial lesion associated with previous attacks of inflammatory rheumatism. At autopsy the diagnosis was verified in both cases; the influenza bacillus was the only organism present and they were found in great numbers; and sections showed them deeply situated in the endocardium at the seat of the disease. Horder believed that the infection had taken place through the lungs, although there was no evidence of a definite attack of influenza. In both cases a leukocytosis was present. In one, that of an adult, the highest count was 18,400; in the other, a boy, the highest count was 22,400.

Smith<sup>10</sup> has described a case very similar to the above. The influenza bacillus was grown from the blood in pure culture twenty-seven days before the patient's death. The patient was a man, aged forty-five years, who had a severe attack of influenza eight years previously, and was suspected of having had one or two subsequent attacks. His last illness, which lasted over five months, simulated quite closely enteric fever. There was a bronchitis, an enlarged spleen, quite definite rose spots, loose stools, a leukocyte count of 6300, and an irregular temperature at times reaching 101° to 103°. The Widal test was negative. The autopsy showed a

<sup>8</sup> Arch. gén. de méd., February and March, 1897.

<sup>9</sup> Lancet, 1905, ii, 1473.

<sup>10</sup> Ibid., 1908, i, 1201.

vegetative endocarditis, a pericarditis, and a pleurisy with some effusion, all showing many influenza bacilli.

Spät<sup>11</sup> reports a case beginning as an ordinary attack of influenza, from which the patient recovered sufficiently to attempt to work, but soon was sick again, and after admission to the hospital continued to run a very irregular temperature, the marked rises usually being preceded by a chill, until his death some forty-six days later. The spleen was somewhat enlarged; no rose spots were noted. The leukocytes were 10,600, a loud mitral systolic murmur developed, with some increase in the area of cardiac dulness. Influenza bacilli were grown from the blood ten days before his death. At autopsy there was found a vegetative endocarditis, pleurisy with effusion, and pyonephrosis, from all of which the bacillus was obtained.

Slawyk<sup>12</sup> also has reported a case of general infection with the influenza bacillus, which he grew a few hours before death from the blood, from the cerebrospinal fluid, and from a small abscess on the back of the hand. At autopsy the bacillus was found in the blood, the lung, and in the meningeal exudate.

Brentz and Frye<sup>13</sup> have recorded a case of influenzal infection in a child nearly two years of age, which evidently began as a respiratory infection with bronchopneumonia, and soon became associated with septicemia and meningitis. There was a leukocytosis of 15,600. Influenza bacilli were grown from the blood and from the spinal fluid twenty-four hours before death. The bacilli were also obtained in cultures from the blood and the meningeal exudate at autopsy.

Ghedini<sup>14</sup> seems to have been more successful than any one else in growing the organism from the blood during life, as he obtained it 18 times out of 28 cases. These are described as typical cases of influenzal bronchopneumonia. The cultures were always taken during and in rather the early part of the febrile period. The cases in which the blood proved negative were not so severe a type of the disease. These results correspond very closely with what we find in pneumonia, and suggest that the early observers were more nearly correct than we have supposed.

Thus in all we have been able to collect 30 cases in which the influenza bacillus has been grown from the blood during life. Two complications are to be noted in connection with the case reported, the phlebitis of the right femoral vein and the arthritis of the left wrist. We cannot reasonably doubt that these were specific in origin, the influenza bacillus being present in the blood. Phlebitis with thrombosis we find mentioned not infrequently in the literature in connection with influenza, and Leichtenstern<sup>15</sup> states that it is a relatively frequent occurrence. However, I have found no other

<sup>11</sup> Berl. klin. Woch., 1970, xlv, 1173.

<sup>12</sup> Woman's Medical Journal, 1908, xviii, 73

<sup>13</sup> Centralbl. f. Bacteriol., etc., 1 abt., Jena, 1906-07, xliii.

<sup>14</sup> Nothnagel's Encyclopedia of Practical Medicine (Am. ed.), Influenza, p. 676.

<sup>15</sup> Zeit. f. Hyg., 1898, xxvii, 315.

instance, except the case reported, in which influenza bacilli have been found either in the blood or in the thrombus. As in the case reported, there is usually an increase in the fever, and at times it is accompanied by chills.

A good many cases of influenzal arthritis have been reported, but unfortunately nearly all of them lack a demonstration of the bacillus in culture. Lord<sup>16</sup> states that no special relation has been established between arthritis and influenza. Dudgeon and Adams<sup>17</sup> however, have reported a case in which the influenza bacillus was grown from the pus obtained from the elbow-joint, and after death a pure culture of the same organism was obtained from the pus from the hip-joint. According to Franke<sup>18</sup> these cases of influenzal arthritis for the most part run a favorable course and recover completely.

**PATHOGENESIS.** There is very little evidence to show that a general infection by the influenza bacillus can be produced experimentally in animals, although Saathoff<sup>19</sup> reports having produced the condition in rabbits to a moderate degree. Pfeiffer, after a long series of experiments on animals was unable to produce a true infection excepting perhaps in apes, in which at least some involvement of the nasal mucous membranes was obtained. As a rule, the symptoms produced were evidently due to the toxins contained in the organisms. Contani<sup>20</sup> believes that the nervous system is especially favorable for the growth of this organism, and he succeeded in producing a well-defined meningitis in rabbits.

The portal of entry of the influenza bacillus into the blood is undoubtedly the lungs in the majority of cases. Usually there has been present some severe infection of the lungs, such as bronchopneumonia. Jehle believes that at least in some of his cases the tonsils were the portal of entry. In a few instances there has been no evidence as to the possible mode of entrance. A primary focus in any part of the body doubtless could afford the opportunity for the organism to invade the blood.

**SYMPTOMATOLOGY.**—On the whole, the clinical picture of influenzal septicemia resembles that of other forms of septicemia. The symptoms are due to an intoxication, as are those of simple toxemia, which represents the ordinary case. Usually there is profound prostration, lack of appetite, severe headache, and marked general pains. The temperature is usually very irregular, and at times there may be two or more sudden rises, frequently accompanied by a chill, during twenty-four hours. Again, there may be an intermission of more than a day, and a malarial temperature may be more or less simulated. In still other cases the temperature curve may resemble very closely that of the ordinary case of typhoid fever. The onset of complications, as a rule, increases the temperature, which may be accompanied

<sup>16</sup> Osler's Modern Medicine, ii, 482.

<sup>18</sup> Deutsch. Zeit. f. Chir., 1906, lxxxv, 335.

<sup>20</sup> Zeit. f. Hyg., 1896, xxiii, 265.

<sup>17</sup> Lancet, London, 1907, ii, 684.

<sup>19</sup> Munch. med. Woch., 1907, liv, 2220.

by chills. The spleen usually is moderately enlarged and in some cases has been palpable. Quite distinct rose spots are at times present. They were noted in Smith's case, and Monie<sup>21</sup> and others have seen rose spots in connection with the so-called typhoid form of influenza. With ordinary influenza the leukocytes do not exceed 12,000 in 70 per cent. of the cases, and not infrequently they are much lower. On the other hand, the leukocyte count may reach as high as 35,000. In the reported cases of influenzal septicemia the observations are too meagre and insufficient for trustworthy conclusions. Horder's highest count was 22,400; Smith's was 6300; Spät's, 10,600; Bentz' and Frye's, 15,600; and in my case the only count made was 7500. Diarrhœa is present at times, and was noted in Smith case. The urine has not shown important abnormalities except in Spät's case, in which a pyonephrosis was present. Here the urine showed albumin, hyaline and granular casts, and a good many pus cells.

**PROGNOSIS.** Judging from the cases so far reported, the outlook in this condition is extremely grave. With the exception of Ghedini's cases, which were less severe, all of the collected cases resulted in death with the exception of mine. Possibly further observation will show, as in Ghedini's series, that in the average case the blood is not infrequently invaded, but followed by prompt recovery.

**DIAGNOSIS.** The diagnosis in these cases must rest entirely upon the demonstration of the bacilli in cultures from the blood; unfortunately this is not without its difficulties. Ordinary media may be used, as hemoglobin is always supplied. Many now prefer a flask containing about 50 c.c. of bouillon, and into this may be injected about 10 c.c. of the blood to be examined. After incubation at 37° to 38° C. for one to three days, blood agar tubes or plates may be inoculated from this.

Clinically these cases resemble no disease so much, perhaps, as typhoid fever; in fact, the resemblance may be almost complete, showing an enlarged spleen and characteristic rose spots. A blood culture alone will decide the matter. In the literature one finds reports of cases of influenza followed by typhoid fever, such as have been reported by Anders,<sup>22</sup> Da Costa,<sup>23</sup> and others. One cannot doubt that both diseases may occur together, or that typhoid fever may follow influenza, but in the absence of accurate bacteriological examinations of the blood one may be pardoned for suggesting that at least in some of these cases there may have been a general infection by the influenza bacillus. Again, certain obscure forms of fever, such as one meets at times, and especially at periods when influenza is prevalent, may have their explanation in a general influenzal infection. We are much in need of more careful observations on the blood in this disease. Ghedini's observations in regard to the

<sup>21</sup> Bull. Med., Paris, xv, 154.

<sup>22</sup> Medical News, New York, 1896, lxxviii, 337.

<sup>23</sup> University Medical Magazine, Philadelphia, February, 1894.

frequency of this bacillus in the blood are quite parallel to what of late years we have been finding in the blood in cases of lobar pneumonia.

**TREATMENT.** In the treatment of this disease we have as yet no specific. The main hope of the future is that some successful serum will be obtained. Cantani<sup>24</sup> and Latapie<sup>25</sup> have produced serums against this infection, and in some cases these were thought to be of some value in experimental infections, but I am not aware that any serum has been used clinically.

Homologous vaccines should be given a trial when they can be obtained, especially in such cases as those reported by Horder and Smith. Thompson<sup>26</sup> and Barr<sup>27</sup> have recently reported good results with vaccines in several cases of streptococcic endocarditis with septicemia.

In the general management of these cases one may follow the methods in vogue in treating typhoid fever in regard to hygiene, rest in bed, diet, and hydrotherapy, though, as a rule, influenzal patients do not tolerate well the application of cold. Convalescence should be carefully managed. They need especially fresh air and nutritious food. It may take weeks or months before the patient is entirely recovered.

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## ACUTE PNEUMOCOCCIC MENINGITIS.

WITH THE REPORT OF A CASE SECONDARY TO EMPYEMA OF  
THE FRONTAL SINUS.

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INFLAMMATIONS of the pia-arachnoid due to *Micrococcus pneumoniae* are not uncommon. Infections of the meninges with this bacterium are invariably fatal, and consequently the disease is of very great interest. Among 49,028 clinical cases of pneumonia, meningitis occurred in 206, or 0.24 per cent., and at necropsy meningitis was noted in 180 out of 4833 cases of pneumonia, or 3.5 per

<sup>24</sup> Zeit. f. Hyg., xlii, 504.

<sup>26</sup> AMER. JOUR. MED. SCI., 1909, cxxxviii, 169.

<sup>25</sup> C. R. Soc. Biol., Iv, 1272.

<sup>27</sup> Lancet, February 23, 1905.

cent.<sup>1</sup> Osler<sup>2</sup> found the pneumococcus in 8 out of 100 necropsies, Aufrech<sup>3</sup> in 7 out of 253 necropsies, and Pearce<sup>4</sup> in 2 out of 121 necropsies on cases of pneumonia. Jundell<sup>5</sup> reports this bacterium in 106 out of 387 cases of acute meningitis. Councilman<sup>6</sup> reports the pneumococcus in 18 out of 61 sporadic cases of meningitis since 1897, and Libman<sup>7</sup> in 6, as secondary infections, out of 100 cases of meningitis.

In regard to the question as to the frequency of primary pneumococcic meningitis, it may be stated that infections of this character are extremely rare. The fact that meningitis so rarely occurs in pneumonia, when in most cases the bacteria are in the blood, gives ample proof of the fact that the microorganisms do not possess any special affinity for the meninges, as is the case with *Micrococcus intracellularis meningitidis*. Councilman<sup>8</sup> reports a series of 28 cases of meningitis due to the pneumococcus, with the possible primary infection in only 3 cases.

There is a difference of opinion as to whether the pneumococcus may cause epidemics of meningitis. Weichselbaum and Netter both believe that this bacterium may give rise to epidemics, and that it is a very frequent cause of both primary and secondary meningitis. Elser and Huntoon,<sup>9</sup> in their recent exhaustive studies on meningitis, in which they reviewed the work of Schotmüller,<sup>10</sup> do not think that the pneumococcus is capable of inciting an epidemic, and also hold the view that most infections occur secondary to some other pathological process produced in the body by the pneumococcus. It seems probable that those epidemics which have been reported as not being due to *Micrococcus intracellularis meningitidis* were due to bacteria other than the pneumococcus. In the early studies on meningitis considerable confusion occurred in regard to the differentiation of *Micrococcus intracellularis meningitidis*, *Micrococcus pneumoniae*, *Streptococcus pyogenes*, *Streptococcus mucosus capsulatus*, etc., due to inadequate methods.

Pneumococcic meningitis usually occurs secondary to some other infectious process in the body, such as pneumonia, otitis media, mastoiditis, and occasionally in ethmoiditis following natural and operative infections, and in infected wounds following fractures at the base of the skull. In extending to the brain from the ethmoid cells the infection usually passes through the cribriform plate. The case reported by Councilman<sup>11</sup> is typical of this mode of infection.

The case of pneumococcic meningitis which we wish to report

<sup>1</sup> Musser and Norris, Osler, *Modern Medicine*, ii, 614.

<sup>2</sup> *Ibid.*, ii, 559.

<sup>3</sup> *Ibid.*

<sup>4</sup> *Ibid.*

<sup>5</sup> *Nordiskt. Med. Arch.*, 1901, v, 2.

<sup>6</sup> *Jour. Amer. Med. Assoc.*, 1905, xlv, 997.

<sup>7</sup> *Mt. Sinai Hospital Reports*, 1903, iii, 546. Cited by Elser and Huntoon.

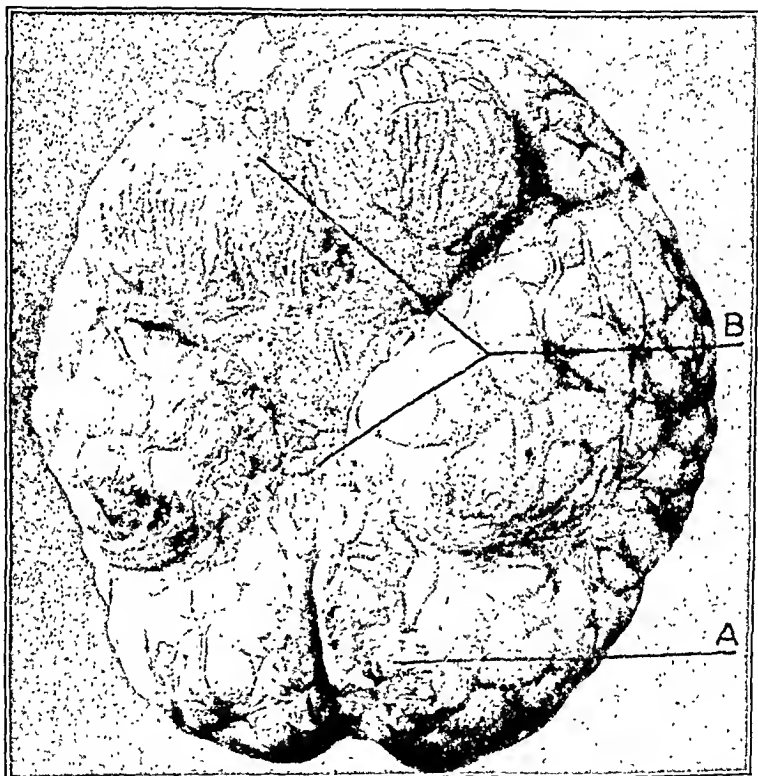
<sup>8</sup> *Jour. Amer. Med. Assoc.*, 1905, xlv, 997.

<sup>9</sup> *Jour. Med. Research*, 1909, xx, 532.

<sup>10</sup> *Munch. med. Woch.*, 1905, lii, 1617, 1683, 1729.

<sup>11</sup> *Loc. cit.*

is one which was secondary to an inflammation of the anterior ethmoidal cell and an empyema of the frontal sinus. In this case the frontal sinus extended over the right orbit, the frontal bone was eroded over a small area, and the meninges were infected from this point (see figure). There was no evidence of the infection passing through the cribiform plate of the ethmoid which was the most advantageous point of entrance, as was shown by its relation to the inflammation in the anterior ethmoidal cell. The infection evidently passed to the anterior ethmoidal cell from the nares by way of the infundibulum and thence through the foramen into the frontal sinus.



Acute pneumococcic meningitis. A, the point of primary infection over the right orbit; B, the area of basilar meningitis surrounded by greenish-yellow pyogenic exudate.

*History.* F. F., male, aged eighteen years, white, single, box maker, was admitted to Columbus State Hospital, June 4, 1909, with a diagnosis of acute mania by the physicians signing the commitment papers. The present attack began four days previously. He had one previous attack which lasted six weeks according to commitment papers.

*Status Præsens.* The patient is in a marked delirium. When pressed with questions he answers them incoherently. The body

is well nourished and the musculature good. The pupils are unequally dilated, the right being completely dilated and immobile. The right upper lid shows marked ptosis and the right eyeball is immobile. All reflexes are exaggerated and the skin is hyperesthetic. The lips are surrounded by herpes, and tongue and teeth covered with sordes. The tongue is heavily coated. The patient's head is drawn to the right and posteriorly. Attempts to move the head in the opposite direction elicit great pain. The back is rigid and shows a slight opisthotonos. There is slight rigidity in the right shoulder joint. Kernig's sign is present in both legs. The skin is cyanotic over extremities and there is a slight petechial rash over both thighs and legs. The bladder is distended; 900 c.c. of dark amber urine was withdrawn per catheter. The respirations are 22 per minute. The respiratory system is otherwise negative except for a slight dyspnoea and slight vesicular breathing. The area of heart dulness is slightly increased. No murmurs are heard. The rate of the heart is 160 per minute. The skin shows *tache cerebrale* and cyanosis. The abdomen is distended and tender on deep pressure. The digestive and genito-urinary systems are negative.

The patient was taken to the operating room at 4 P.M. and a lumbar puncture made for the diagnosis of cause of the meningitis.

The results of the various analyses are as follows:

*Urine.* Amber, slightly clouded, specific gravity 1026, acid, albumin 1.5 grams to the liter. Few granular and epithelial casts, few polymorphonuclear leukocytes and erythrocytes, mucous threads. Otherwise negative.

*Blood.* Erythrocytes, 5,760,000; leukocytes, 33,200. Hemoglobin (Sahli), 100 per cent. Differential: large mononuclears, 2.78 per cent., small mononuclears, 4.4 per cent., polymorphonuclears, 92.8 per cent. Few free nuclei.

*Cerebrospinal Fluid.* Three c.c. withdrawn, clouded; globulin increased. Large numbers of polymorphonuclear leukocytes. Large numbers of Gram-positive diplococci, free and phagocytized. These microorganisms are typical pneumococci, as was shown by capsules and also later by cultures.

*Diagnosis.* Acute pneumococcic meningitis.

The usual therapeutic measures for the relief of meningeal inflammation were applied. The patient died at 5 A.M., June 5, having been in the hospital seventeen hours.

The necropsy was performed five hours post mortem and showed the following conditions:

*Necropsy Report.* Rigor mortis is present. The pleural cavity shows numerous fibrinous adhesions over the upper lobe of the right lung. Both lungs are slightly increased in weight and show slight passive congestion. There is a marked increase in the fluid in the pericardial cavity. The heart is normal. Peritoneum is normal.



The liver is distinctly mottled in appearance and shows marked fatty infiltration together with passive congestion and cloudy swelling. The gall-bladder is normal. The spleen shows a slight passive congestion. The kidneys are enlarged, mottled and lobulated, and the cortex thickened. Microscopic examination reveals acute parenchymatous nephritis. The adrenals are slightly congested. The stomach and intestines are distended with gas and show slight passive congestion. The bladder is distended. The mucosa is slightly congested. The genitals are normal.

A detailed examination of the head and spine reveals the following:

The scalp is of normal thickness and strips easily. There is a slight contusion in right frontal region. The calvarium is normal. The brain weighs 1200 grams. The dura is distended, injected, and the convolutions are barely visible. A large amount of fluid escapes on opening the dura. Cultures and slides show *Micrococcus pneumoniae*. The dura is adherent over the orbit in the region of the right frontal sinus. There is an erosion in the frontal bone over the orbit 1.5 cm. to 2 cm., and the opening extends into the sinus. There are marked fibrinous adhesions in this area between the bone, dura, and pia-arachnoid. An inflammatory exudate is also noted. The pia-arachnoid is intensely congested. Fibrinous inflammatory exudate with adhesions is noted along the right olfactory tract to the optic chiasm, back of which the entire base of the brain, including the crura, pons, medulla, etc., are surrounded by the same greenish-yellow, fibrinous exudate. This exudate seems to be limited to the base of the brain, with the exception of the cisterna magna, which contains some exudate, and extends down the cord. The ventricles contain an increased amount of very cloudy fluid. There is a very marked increase in the total cerebrospinal fluid. Pneumococci are very prevalent.

Spinal cord: The dura is adherent to the pia-arachnoid its entire length by means of fibrinous adhesions. The pia-arachnoid is markedly injected. Greenish-yellow, fibrinous exudate is abundant.

Middle ears: normal.

Frontal sinus: The left side is normal, the right side shows an erosion of the frontal bone over the sinus. The right frontal sinus is larger than the left and is filled with inflammatory exudate. It extends well over the right orbit. The mucous membrane is inflamed and necrotic. There is a foramen between the frontal sinus and the anterior ethmoidal cell. This foramen is filled with greenish-yellow exudate. Cultures and slides show *Micrococcus pneumoniae*.

Anterior ethmoidal cell: The left is normal, the right shows a slight amount of inflammatory exudate similar to that noted

in the frontal sinus. Cultures and slides show *Micrococcus pneumoniae*.

Middle and posterior ethmoidal cells: normal.

Sphenoidal sinus: normal.

Nares: normal.

*Anatomical Diagnosis.* Acute pneumococcic meningitis, empyema of the right frontal sinus, with slight involvement of the anterior ethmoidal cell, acute parenchymatous nephritis, fatty infiltration of the liver, passive congestion of the lungs, liver, kidney, spleen, intestines, etc., pericardial effusion, cloudy swelling of the liver.

*Examination of the tissues from the nervous system and discussion of the pathology of pneumococcic meningitis.* The base of the brain shows the most marked lesions. The exudate, which is markedly cellular and fibrinous, extends from the anterior portion of the lower aspect of the right frontal lobe back over the optic chiasm, crura, pons, and medulla down the spinal cord. The exudate is almost entirely confined to the base of the brain and extends deep into the sulci. There is no exudate along the longitudinal fissure. There is an intense injection of all vessels. The meninges of the cerebellum are intensely congested, which is quite characteristic of pneumococcic meningitis. The cranial nerves, particularly the third, show evidences of inflammation. The Gasserian ganglion is swollen. The ventricles show an increase of fluid and a slight amount of exudate. The microscopic examination of the tissues shows the following:

The neuroglia in the subpia is slightly increased. This is characteristic of this form of meningitis, especially in those cases lasting from ten to fifteen days, as is pointed out by Southard and Keene.<sup>12</sup> The cortical tissue is infiltrated with polymorphonuclear leukocytes, and large endothelial phagocytic cells, similar to those described by Councilman,<sup>13</sup> are noted in the region of the blood-vessels. This condition occurs in practically all forms of meningitis. The arteries at the base of the brain show a peculiar infiltration with leukocytes and a pushing up of the intima from the media with the fibrinous exudate. The veins show an infiltration with leukocytes in some places, but no other change in the walls. The cranial nerves and the Gasserian ganglion show a direct extension of the exudative inflammatory process from the brain. The right third nerve shows a slight increase in neuroglia. Changes of this character are said to be most marked in pneumococcic meningitis of long standing.

This case is typical of practically all cases of pneumococcic meningitis. The following points may be noted in regard to this disease:

- (1) Its virulent and fatal character; 99 per cent. of all cases die.
- (2) The greenish-yellow character of the exudate, which is markedly

<sup>12</sup> Jour. Amer. Med. Assoc., 1906, xlv, 13.

<sup>13</sup> Ibid., 1905, xlv, 997.

cellular and fibrinous in constitution. (3) The polymorphonuclear and endothelial cell infiltration of the cortex of the brain. This change is, on the whole, less marked than in the other forms of meningitis. (4) The increase in neuroglia in the subpia and in the cranial nerves. (5) The infiltration of the walls of the arteries with leukocytes and exudate, causing a spreading apart of the intima and media and in addition the infiltration of the veins with leukocytes.

## SEROUS MENINGITIS IN TYPHOID FEVER AND ITS TREATMENT BY LUMBAR PUNCTURE.

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THE object of this communication is to draw attention to a symptom complex occurring in the initial stage or during the course of typhoid fever, called by some by the generic name of typhoid-meningitis, and by others the cerebrospinal type of typhoid fever. German authors designate the condition as meningotyphus. These names, moreover, are intended to include cases of true purulent meningitis caused by *Bacillus typhosus*, as well as those cases of typhoid fever with meningeal symptoms in which the serous fluid is found sterile after careful bacteriological investigation by culture, etc. They do not include those cases of cerebrospinal inflammations, during the course of typhoid fever, caused by other than the bacterium of Eberth. The term meningeal irritation, or meningism,<sup>1</sup> is generally reserved for those cases in which an anatomical substratum is supposed not to exist. Meningism is a very popular term with French authors. It is nothing more than a very striking clinical phase of certain infectious diseases occurring in the exanthemas, in typhoid fever, pneumonia, etc. Meningism may usher in these diseases, or it may develop during their course. It usually disappears after a short time. If the case ends fatally, a pathological basis for this condition of meningism or meningeal irritation cannot be found at autopsy.

According to Osler, "Cortical meningitis is not to be recognized by any symptom or set of symptoms from a condition which may be produced by the poison of many of the specific fevers." In other words, meningism and meningitis may be clinically identical.

My own observations comprise three cases observed at the German Hospital, in which a serous exudate was found in the subarachnoid space of the cord by means of lumbar puncture. In one case the

<sup>1</sup> This term was introduced by Dupré. Discussion on this subject in the article by Troisier, Bull. et mém. des Hôp. de Paris, xvii, 1900.

evacuation of this spinal fluid saved the patient from imminent death. These three cases, judging from the character of the evacuated fluid belong to the group which has been styled by Quinke meningitis serosa acuta. After the experience which I had made with the above-mentioned case, I was awakened to the importance of meningeal signs in typhoid fever and their effective treatment by spinal puncture. My position is similar to that of Georg Boeninghaus,<sup>2</sup> the author of the monograph on acute serous meningitis, who, in a case of suspected abscess of the brain, of otitic origin, after trephining, saved his patient's life by evacuating serous fluid from the ventricles of the brain by puncture. Brain abscess was not present.

A frank recital of my cases, with special reference to the clinical import of meningeal symptoms in typhoid fever, was at first intended. A review of the literature, however, showed that with the exception of Cole and MacCallum's<sup>3</sup> excellent work, done at the Johns Hopkins Hospital, there exists no comprehensive article on this subject. The treatise of Hare and Beardsly<sup>4</sup> only appeared a short time ago, the last edition being published ten years ago. It was therefore deemed advisable to make a more general study of the subject. I have also been able to add a number of articles, not mentioned by Dr. Cole and Dr. Hare.

The state of our knowledge of typhoid meningitis resolves itself naturally into three different periods: (1) Cases recorded by the old clinicians before the bacteriological era. These include, indiscriminately, cases of typhoid fever with meningitic symptoms, as well as a large variety of cases in which the meningitis arose as a complication brought about by suppurative processes of organs in close proximity with the brain, such as the ear and the frontal sinus. Or, the meningitis was a part symptom of a general sepsis, or finally the typhoid fever and the meningitis partook of the nature of two separate infections. Thus, in two epidemics of cerebrospinal meningitis in Hamburg, Curschmann observed a number of cases of typhoid fever which clinically presented the appearance of the then epidemic cerebrospinal fever. Curschmann suspects that this type of typhoid fever may have been caused by a double infection of typhoid fever and cerebrospinal meningitis.

The second period of our knowledge of this subject begins with the bacteriological investigation of the brain, cord, and meninges. In Curschmann's unique case of ascending (Landry's) paralysis in the course of a case of typhoid fever, that author<sup>5</sup> was enabled to show for the first time the presence of the typhoid bacillus in the

<sup>2</sup> Meningitis Acuta Serosa, 1897.

<sup>3</sup> Johns Hopkins Hospital Reports, 1904, xii, 379.

<sup>4</sup> The Medical Complications and Sequelae of Typhoid Fever, second edition, September, 1909.

<sup>5</sup> Nothnagel Series, vol. iii, part i, p. 259, and Congress f. innere Medizin, 1886, Band vi, p. 469.

tissue of the cord. That meningitis may occur as a concomitant process during the course of typhoid fever was confirmed by Bernhard<sup>6</sup> who at the same time pointed out the work of Fritz<sup>7</sup> a French physician whose publications on that subject had preceded Curschmann's but had not become generally known. Felix Wolff<sup>8</sup> then published a series of twelve cases from Curschmann's service in the Hamburg General Hospital. A further contribution to the pathology of this subject was then given by Fr. Schulze<sup>9</sup> at Erb's clinic in Heidelberg. He made a careful study of a case of typhoid fever accompanied by severe meningeal symptoms, to which the patient finally succumbed. At autopsy however, certain inflammatory changes were found especially on the vessels of the pia and arachnoid of the cord and brain, the latter organ showing very little, if any change. The fluid in the ventricles of the brain was clear, a purulent meningitis could not be found, nor did the gross appearance or the microscopic examination of the brain or cord explain the fatal ending of this case.

Still a further contribution was that by A. Hoffmann.<sup>10</sup> His case presented clinically all the true characteristic signs of a purulent meningitis in a well-marked case of typhoid fever; opisthotonos, spastic extremities, tremor, coma, and clonic convulsions developed. The patient evidently died from the effects of the cerebrospinal complications. At autopsy the fluid of the ventricles was clear. There was oedema of the pia and arachnoid.

In addition to this was found round-cell infiltration along the vessels of the pia and arachnoid tissues, as well as along the vessels of the cortex. *Bacillus typhosus* was found in the fluid as well as in the substance of the coverings of the brain and cord. The author looks upon this case as an example of a meningitis directly due to an invasion of the *bacillus typhosus* into the covering membranes of the brain and spinal cord. He considers the serous exudate of the meninges and the ventricles as the first stage of a suppurative meningitis.

A. Loeb,<sup>11</sup> of Erb's clinic in Heidelberg, describes a case of serous meningitis in typhoid fever accompanied by papillitis and dilatation of the vessels of the retina. The patient showed opisthotonos, coma, increased knee reflexes, and Trousseau's phenomenon. An attempt was made to perform lumbar puncture, but failed; gradual recovery followed. This article is a very extensive literary study, going into all the details of the clinical features of typhoid meningitis. In an article entitled "On Symptoms of Cerebral Pressure in Typhoid Fever," H.

<sup>6</sup> Berl. klin. Woch., 1886, No. 50.

<sup>7</sup> Études cliniques . . . dans la fièvre typhoid, Paris, 1864.

<sup>8</sup> Deut. Archiv f. klin. Med., Band xliii.

<sup>9</sup> Congress f. innere Medizin, 1897, Band vi, 393.

<sup>10</sup> Deut. med. Woch., July 12, 1900.

<sup>11</sup> Deut. Arch. f. klin. med., Band lxii, 211

Salomon,<sup>12</sup> of von Noorden's clinic in Frankfort, describes a number of cases, which in the initial stage of the fever presented signs of hyperemia in the fundus of the eyes: there was capillary injection in the papilla, the edges looked indistinct, the veins of the retina were dilated and convoluted. Lumbar puncture was made. The liquor cerebrospinalis was sterile and did not agglutinate the typhoid bacillus. The author refers the changes which were found in the fundus of the eye to the pressure exerted by the intra-meningeal exudation. This condition, is, according to him, the direct effect of a serous meningitis.

The third and final stage of our knowledge of this subject begins with the publications of Quinke in 1891, and the universal employment of lumbar puncture in practice. Although this procedure is at present used as one of the routine means of investigation both for diagnostic and therapeutic purposes, we hear very little of its use in connection with the subject under consideration here. This may perhaps be due to the fact that we are inclined to explain the cerebral symptoms occurring in the course of typhoid fever, invariably on the basis of a toxemia, and have neglected to apply lumbar puncture, not expecting to find in the cerebrospinal fluid, in the character of the exudate or transudate, in the bacteriological findings of that fluid, or finally in other still unknown factors, any clue to the cerebral or spinal symptoms by which the disease is characterized.

A comprehensive study of typhoid meningitis with a detailed and tabulated citation of cases from the literature was made by R. I. Cole and W. J. MacCallum. Cole divides the cases into three groups:

Group I. Cases with symptoms of meningitis in which no meningeal lesions were demonstrated or in which no definite relationship between the bacteria and the symptoms are found. This group comes under the heading of meningism.

Group II. Cases showing symptoms of meningitis in which the relationship of *Bacillus typhosus* was demonstrated by its cultivation from the cerebrospinal fluid during life, or at autopsy, and in which the demonstrated lesions were not of a suppurative character.

Group III. Cases of purulent meningitis (caused by the sole presence of *Bacillus typhosus* in the exudate).<sup>13</sup>

I am concerned here with the two first groups only, and would say that the term meningism is not identical with the meningotyphus of German authors, as Cole seems to imply. In the German literature typhoid meningitis stands for a clinical type of fever, the pathological basis of which is either a serous or a suppurative inflammation caused by the bacillus of Eberth. Meningism, on the other hand, is reserved for those cases in which a suppurative meningitis is not present, or in which at autopsy the cord and brain show no patho-

<sup>12</sup> Berl. klin. Woch., 1900, No. 6.

<sup>13</sup> The words in parentheses are mine.—R. S.

logical changes. We cannot at present dispense with this term. In looking critically into the French and Italian literature of cases recorded under that name, it will be observed that in many instances lumbar puncture was not done. Furthermore, in the absence of bacteriological investigation and autopsy findings (in the majority of the observations), it is a question, whether these cases were simply examples of meningism or whether they did not rather belong to the group of serous meningitis.

An interesting case of serous meningitis is also reported by Boden,<sup>14</sup> of Cologne. A child, aged fourteen years, was admitted to the hospital at the end of the first week of typhoid fever. Hyperesthesia of the body, cyanosis. Two days later, severe epileptic attack, deep stupor, loss of patellar reflex. Left-sided abducens and facial paralysis. Loss of pupillary reflex. Death occurred three days later. Autopsy: Marked typhoid fever. Meningitis serosa. A large amount of clear serum was present at the base of the brain. The brain itself was normal. The ventricles were distended. From the fluid in the ventricles a pure culture of the bacillus of Eberth was obtained. The fluid also gave the Widal test. Two cases of serous meningitis in children, with recovery, treated by spinal puncture, are reported by Francis Huber.<sup>15</sup>

According to Quincke's<sup>16</sup> experience in many infectious diseases, such as typhoid and scarlet fever, pneumonia and other unclassified febrile affections, nervous symptoms may predominate to such a degree that the observer is easily led to accept local changes in the central nervous system. On investigation, however, gross pathological changes are not apparent. Lumbar puncture shows an increase of the spinal pressure or of the cellular elements of the spinal fluid. Although serous exudates must not necessarily be caused by the presence of bacteria, we sometimes find in such cases the meningo-, pneumo-, or streptococcus, the typhoid-, coli-, or influenza bacillus. That the bacteria did not as usual lead to a purulent inflammation may be due to their small number or diminished virulence, or to the short duration of the attack. In such cases we must accept the theory that the above mentioned bacteria produce a serous meningitis. The rise in pressure without the bacteria may be accounted for by the clinical irritation of the meninges, which in its turn is due to the toxins of the bacteria. Finally, in those cases in which there is no increase of pressure of the cerebrospinal fluid, we must make the influence of the toxins on the cerebrospinal system accountable for the nervous symptoms.

In the acute serous exudates, Quincke adds, the lumbar puncture has a decided therapeutic effect. "By means of one or two punctures,

<sup>14</sup> Münch. med. Woch., February 28, 1897.

<sup>15</sup> Arch. of Pediatrics, 1894, p. 5.

<sup>16</sup> Deut. med. Woch., 1905, No. 46, p. 1825.

at times a definite decisive turn for the better may be brought about, in the course of an acute affection."

My own cases are as follows:

CASE I.—D. M., a civil engineer, aged twenty-three years, was brought to the private wards of the German Hospital, on October 6, 1907. The previous history of the patient has no bearing on the case. The present history shows that he has been surveying in the northern part of the State, was in the fields all day, and drank water indiscriminately. Status: A well nourished, muscular individual. Has complained of headaches for a week or ten days. Patient is listless. Temperature,  $105^{\circ}$ ; pulse under 100. Patient has diarrhoea, repeated nose-bleed. Physical examination: Coated tongue, abdomen not distended, no rose-spots. Examination of the heart reveals: Moderate distention to the right and left. Loud blowing systolic murmur at the apex. Diffuse bronchitis. Slight dulness on the right chest, posterior inferior. The spleen not palpable. Urine, no albumin. Diazo reaction. Blood examination: Leukopenia, no eosinophiles. Widal suggestive.

*Diagnosis.* Typhoid fever in the second week. Compensated mitral insufficiency, bronchitis, infiltration of the lower lobe of the right lung. The routine treatment for typhoid fever was applied. Appropriate heart stimulation on indication.

The principal features of the case within the next ten days were as follows:

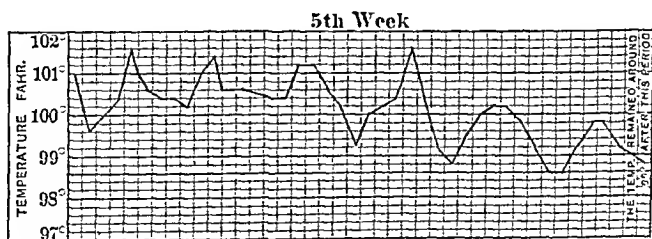
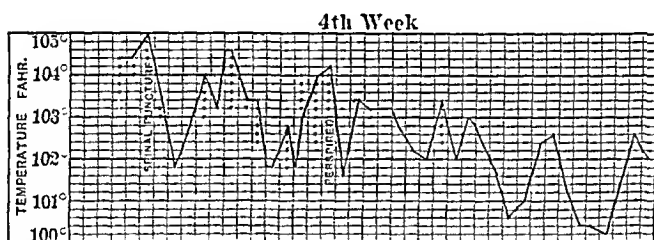
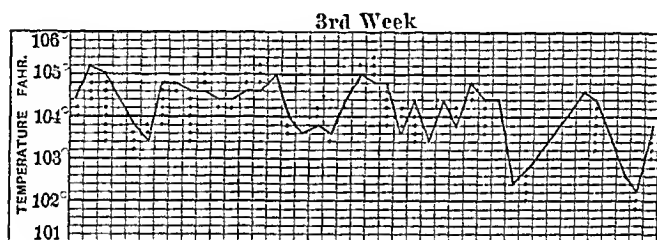
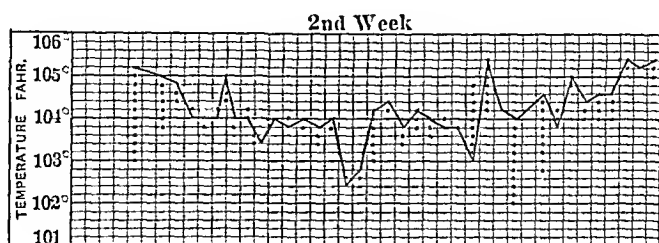
The patient became more and more drowsy, and had to be awakened when nourishment was given. The cough was very troublesome. Free expectoration. Patient was markedly delirious. The temperature remained pretty steadily around  $105^{\circ}$ . Remissions under use of the cold sponge and pack. The physical examination now showed that an extended pneumonia of the right lung had developed, with a metapneumonic exudate. The typhoid bacillus was not present in the sputum. The pulse at times distinctly dicrotic. Both respiration and pulse quite irregular at intervals. Toward the end of the third week the cerebrospinal symptoms became more and more marked. The patient lapsed into a deep coma, from which he could hardly be roused. The nights, however, were very restless, the patient at times becoming wildly delirious. He made several attempts to get out of bed. Micturition and defecation involuntary; nausea and vomiting. There developed very marked stiffness of the neck; knee reflexes greatly exaggerated; the patient's upper and lower extremities were held in hyperextension, and showed decided tremor. Foot clonus. Abdomen more and more distended. It became impossible to feed patient. Trismus.

Although the temperature showed some tendency to remission, it reached  $105^{\circ}$  on the nineteenth day. Both pulse and respirations became very irregular, and the pulse at times was weak and fluttering. The patient's condition seemed very grave; and as the cerebro-



spinal symptoms became more and more marked, lumbar puncture was made, and 40 c.c. of a perfectly clear fluid withdrawn.

The apparent effect on the temperature was very striking, as is shown by the accompanying charts. The patient recovered gradually



The temperature record in Case I, by weeks of the disease.

from his coma. The spinal symptoms also gradually decreased, and disappeared completely within the next few days, and therefore a second puncture was not considered indicated. The effect of the puncture seemed such that the patient lapsed into a

natural sleep. The abdomen became flat, and the patient was again able to take food. Having reached the fourth week of the attack, the remittent stage having already begun, as is shown by the charts, his condition improved from day to day. He perspired very freely. Resolution of his pneumonia had set in at this time. In the fifth week otitis media of the left side developed; somewhat later, periostitis of the left tibia. Both conditions cleared up without further trouble.

The microscopic examination of the spinal fluid showed the absence of cellular elements in the centrifugal specimen. No bacteria in the hanging drop. Cultures tending to prove the presence of the typhoid bacillus were negative. The serum was not tested for the Widal reaction.

CASES II and III.—I have since then observed two other cases in male patients showing symptoms of typhoid meningitis during my summer service of last year. One case was punctured twice, the other case three times. The objective as well as the subjective symptoms of one case completely receded. The patient died later from intestinal hemorrhage. The third case was one of protracted delirium and coma. The physical signs of meningitis were well marked in this case, and these as well as the psychic symptoms seemed to be favorably influenced by this procedure. From 20 to 40 c.c. of a perfectly clear spinal fluid was removed each time. This had no sediment, and cultures were negative. The serum reaction was not made, nor was the spinal pressure determined.

As regards the clinical features of typhoid meningitis, of special interest are those cases of typhoid fever which come under observation with the predominant symptoms of meningitis. In this connection I must mention those remarkable cases, examples of which are reported from time to time, in which the meninges are the sole seat of localization of the typhoid infection without any of the usual lesions of the typhoid process in the intestines or other organs. The first consideration will naturally be that of a precise diagnosis, with all the methods at present at our command. The prognosis and treatment are also determined from the results of this investigation. Cytological, bacteriological, agglutination tests must be carefully made in order to be able to demonstrate, if possible, whether we are dealing with a case of typhoid fever, or cerebrospinal, tubercular, or other variety of meningitis. Secondly, attention should be directed to those cases of undoubted typhoid fever in which meningeal symptoms develop. An exploratory puncture should be made. In some cases the psychic symptoms may be the most prominent; in others, cortical symptoms alone may be present; in still others, cerebrospinal symptoms. The fundus of the eye should be carefully examined; the absence or increase of the knee-jerks, as well as the other reflexes, should be carefully noted. The presence of the Kernig sign or of the ankle clonus may alone give the indication for lumbar puncture. Furthermore,

the determination of the pressure of the spinal fluid by Quincke's apparatus, so painstakingly introduced here by Dr. Henry Heimans,<sup>17</sup> should be carried out in the puncture of these cases.

The small number of cases observed by me does not authorize me to draw any general conclusions as to the strict interpretation of serous meningitis in typhoid fever. Nor would it be scientific to draw broad conclusions as to the etiology or treatment of this symptom complex in typhoid fever, judging by analogous conditions found in other acute infectious diseases. I have the impression that in typhoid fever spinal puncture has not as yet been exploited to the extent that its application seems to warrant. In addition to its value as a diagnostic measure, there remains, I think, the crude indication to remove an excess of spinal fluid in the attempt to mitigate symptoms, which, though they may be due in part to the toxemia, may also be ascribed to an excess of pressure on the brain and spinal cord. Finally, I may perhaps be permitted to quote Keen:<sup>18</sup>

"The symptoms of cerebral involvement in typhoid fever, especially of meningitis, are often overlooked. They are marked by the general stupor, and are supposed to be only connected with the usual delirium of typhoid. I am strongly disposed to think that the meningitis accompanying this disease has been frequently overlooked, by reason of the fact that the head is not very often opened in typhoid necropsies unless the cerebral symptoms have been very prominent. Even in cases without marked cerebral symptoms examination of the brain will show meningitis and infection by the bacilli of typhoid fever to be far more frequent than has been supposed heretofore."

I am indebted to Drs. Garbat, McCready, and Spiegelberg, all of the house-staff of the German Hospital for their hearty coöperation in these observations.

<sup>17</sup> The Technique of Lumbar Puncture, with Special Reference to the Pressure of the Cerebrospinal Fluid. N. Y. Medical Journal, November 17, 1906.

<sup>18</sup> Surgical Complications and Sequelæ of Typhoid Fever, 1898, p. 175.

## TUMORS OF THE ACOUSTIC NERVE, THEIR SYMPTOMS AND SURGICAL TREATMENT.

WITH THE REPORT OF A CASE OF COMPLETE RECOVERY AFTER  
OPERATION BY DR. HARVEY CUSHING.

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TUMORS of the cerebellum may be divided into two classes, those involving the hemispheres and the central portion, and those lying upon the base of the brain in the cerebellar pontine angle. While the diagnosis of a tumor within a mass of the cerebellum is not, as a rule, difficult, it is as yet almost impossible to locate exactly the position of such a tumor. Tumors of the acoustic nerve, on the other hand, which occur with about equal frequency with tumors within the cerebellum, are much more readily diagnosticated.

In the early history of brain surgery attempts at removal of tumors in the cerebellum so frequently failed that surgeons became reluctant to undertake this operation. Within the last five years, however, it has been necessary to change this view, and, with the improvement of technique, there have been recorded a large number of successful cases of surgical interference in cerebellar tumors, and more particularly in tumors affecting the acoustic nerve. It seems worth while, therefore, at the present time to present a summary of our knowledge of this subject, to discuss the symptoms and diagnosis of tumors, especially of the acoustic nerve; to collect and analyze cases of operation upon tumors of the cerebellum up to the end of 1909, to discuss their pathology as bearing upon the prognosis of operation, and to describe the technique which has been productive of favorable results. I venture to do this because of my experience in thirteen cases of tumors of the cerebellum, in eleven of which an operation has been undertaken, and because of the fact that I can present a case of perfect recovery ten months after removal of a tumor of the acoustic nerve.

The general symptoms of brain tumor, headache, vertigo, vomiting, and choked disk, which usually appear early in the course of all cerebellar tumors, need no special comment. It is the localizing symptoms which make tumors of the cerebellum, and especially tumors of the acoustic nerve, of particular interest.

**SYMPTOMS OF TUMORS OF THE ACOUSTIC NERVE.** The symptoms which indicate the location of a tumor in the cerebellar pontine angle upon the acoustic nerve may be divided into three classes: (1) Those referable to the cranial nerves; (2) those referable to the involvement of the cerebellar peduncles; and (3) those referable to compression of the tracts passing through the pons.

1. *Symptoms Referable to the Cranial Nerves:*

(a) Slight anesthesia of the face on the side of the tumor, first shown by corneal anesthesia and an absence of the corneal reflex.

(b) Weakness of the external rectus muscle of the eye on the side of the tumor, due to a pressure on the sixth nerve. This may be first noticed by the occurrence of nystagmus on turning the eyes toward the side of the tumor, and later a decided internal strabismus may occur. The eye looks away from the tumor.

(c) A weakness of the muscles of the face on the side of the tumor, first noticeable in a slight disturbance of the act of winking and a slight lack of expression, which is later followed by an actual weakness of all the muscles supplied by the seventh nerve. Pressure on this nerve is rarely, if ever, sufficient, however, to cause a reaction of degeneration in these muscles.

(d) Tinnitus in the ear on the side of the tumor, soon followed by some deafness in the ear, which may be slight and only detected by tests with the Galton whistle, high notes or low notes, or both, being lost. This deafness may be as marked for bone conduction as for ear conduction.

(e) Vertigo, felt by the patient as a sensation of falling toward one side, or as a sensation of rotary movement of the body, both of which symptoms must be ascribed to irritation of the labyrinthine division of the auditory nerve.<sup>1</sup>

(f) Difficulty of swallowing and hoarseness of the voice, owing pressure on the ninth nerve.

(g) Sudden attacks, which may be called vagal attacks, referable to irritation of the tenth nerve, consisting of rapid pulse, sensations of flushing of the body or of the head, sudden faintness without an actual loss of consciousness, attended by more or less vertigo.

(h) Paralysis of the tongue, shown by thickness of speech or difficulty of articulation, and by protrusion of the tongue toward the side of the tumor.

2. *Symptoms Referable to the Involvement of the Cerebellar Peduncles.*  
The second set of symptoms is referable to the compression of the cerebellar hemisphere and its peduncles. The portion of the cerebellum that will necessarily be involved is the flocculus, which projects over the middle peduncle of the cerebellum as it comes from the pons. As we have no means of distinguishing between the functions of different portions of the cerebellum,<sup>2</sup> it is uncertain whether the symptoms of a cerebellar nature are due to destruction

<sup>1</sup> I cannot confirm the statement of Stewart and Holmes (Brain, 1904, p. 525), that in cerebellar tumors the sense of displacement of objects in front of the patient is from the side of the lesion to the opposite side. They also state that when a tumor is within the cerebellum the subjective rotation of self is from the side of the lesion toward the healthy side, but when the tumor is outside the cerebellum the subjective rotation is from the healthy side toward the side of the lesion. Oppenheim has also failed to confirm this assertion.

<sup>2</sup> See Horsley and MacNulty, Brain, January, 1910.

of this flocculus or of the two peduncles entering the cerebellum just under the site of the tumor. These symptoms are:

(a) A staggering gait and feeling of uncertainty of the position of the body in space when supported upon the legs, which causes swaying when the eyes are closed and staggering when the eyes are open, attended by a disagreeable sense of vertigo, which leads the patient to seek support whenever in a standing posture. The direction of the staggering is, in the majority of instances, away from the tumor, although cases have been put on record in which the patient staggered toward the side of the tumor. The direction of the staggering is not to be taken in itself as a very important symptom, but the fact that the patient staggers *uniformly toward one side* is an important symptom of an affection of the peduncles of the cerebellum as they enter the organ, and therefore the existence of staggering in a definite direction, combined with evidences of the implication of the cranial nerves upon one side, is a definite local sign of a tumor in the cerebellar pontine angle.

(b) Another symptom of cerebellar origin is an imperfect muscular tone in the muscles of the arm and leg on the side of the tumor. It is uniformly admitted that the cerebellum has a direct tonic influence upon the muscles, and that this influence is homolateral. This lack of tone is attended by an awkwardness of movement not due to any actual weakness, but to an imperfect coördination of the motions performed. Thus, rapid movements made by both hands or fingers together often prove that the hand on the side of the lesion is moved less freely, rapidly, and skilfully; and other tests may show a true ataxia. There may be also an ataxia of the leg, so that to stand on one foot is impossible. Such an ataxia in the leg may lead to staggering toward the side of the tumor. This symptom has been named diadokokinesis. The maintenance of a proper tone in the muscles appears to have some relation to the response of those muscles to irritation, and it is probably on this account that lesions of the cerebellar peduncles or of the cerebellum are usually attended by a loss of knee-jerk and of the deep reflexes on the side of the lesion; yet this symptom of a loss of reflex on the side of the tumor is not always found in these cases of pontine angular growth. It has been observed, however, in too many cases to allow us to overlook it.

(c) Another symptom of importance due to cerebellar lesion is the abnormal position of the head. Whether this is due to a loss of tone in the muscles of the neck which support the head, or whether it is due to the weight of the tumor, producing instinctive drawing of the head downward toward the side of the tumor, or forward or backward, according to the position of the tumor in relation to the axis of the body, may be left uncertain. A reference to Fig. 1, which shows the position of such a tumor inserted in the diagram of Fraser, will indicate that a tumor at this location is very near to

the centre of gravity of the head, and it can be readily imagined that a tumor growing backward might so disturb the equilibrium of the head as to lead to an abnormal position, which might be backward, but would naturally be more toward the side of the tumor than away from it.

3. *Symptoms Referable to Compression of the Tracts Passing Through the Pons.* A third set of symptoms is to be traced to a compression of the motor tracts and sensory tracts passing through the pons and medulla on their way to and from the limbs of the opposite side. Compression of the pons is very much less likely to cause disturbance in the transmission of sensation than in the transmission of motor impulses, and therefore weakness of a hemiplegic type in the arm and the leg in the side opposite to the tumor is more commonly observed than is anesthesia in the corresponding parts. This weakness is usually attended by an exaggeration of the reflex, by an increase in the knee-jerk, ankle clonus, and Babinski reflex, and such exaggeration is doubly evident because of the loss of the knee-jerk upon the side corresponding to the tumor. This weakness of one leg may intensify the difficulty of walking and may influence very markedly the gait. A patient with a weak leg has something of a tendency to stagger toward the leg that is weak, to use it less freely, and to bend downward toward that side. It has already been remarked that many of these patients stagger away from the tumor, and it is not at all impossible that this direction of the staggering is due to the imperfect use of the leg on the side opposite to the tumor. The actual weakness present in the arm or leg may be easily detected by dynamometer tests, and in many cases has amounted to such a marked hemiplegia that any use of the arm or of the leg was impossible. While anesthesia and analgesia in the limbs of the side opposite to the tumor is much less commonly observed than is paralysis, many patients complain of feelings of numbness, tingling, gooseflesh, or burning in these limbs; and such paresthesias may be followed by an actual disturbance of sensation. In the advanced stages of these cases, in which the patients have died of the tumor, a hemiplegia has developed toward the close of life, not, however, involving the face, and it is in these extreme cases that anesthesia has been observed in the paralyzed limbs.

The diagnosis, therefore, of these tumors is easily made from these three sets of symptoms: (1) Of the cranial nerves; (2) of the cerebellum; and (3) of compression of the sensory and motor tracts.

CASES OF ACOUSTIC TUMORS.: In the following case, which was first recorded in 1893,<sup>3</sup> the diagnosis was quite clear:

<sup>3</sup> AMER. JOUR. MED. SCI., April, 1893.

CASE I.—*Tumor of the acoustic nerve; operation; tumor not found; autopsy.* M., aged thirty years, was under my observation from January, 1890, until December, 1891. When first seen he was suffering from severe frontal and occipital headache, from vertigo, which was much increased by moving the head suddenly or while lying down; from tinnitus aurium, from numbness of the left side of the face and in the mouth, and from a very continuous feeling of drowsiness and dulness. These symptoms had developed gradually during the preceding three years, and within a year he had also noticed double vision and a gradually increasing blindness. His friends said that his speech had become "slow and thick."

He was referred to me by Dr. Weeks, from the Eye Department at the Vanderbilt Clinic, where an examination had shown great prominence of the eyeballs, the left one deviating outward; dilated pupils; marked nystagmus on lateral movements of the eyes; well-marked choked disks; and diminution of all visual fields.

My examination showed that there was some slowness of speech, which was accounted for by his mental dulness, there being no evidence either of aphasia or of paralysis of the tongue. There was no disturbance of sensation, of motion, or of reflex action, and there was no ataxia in the gait. The existence of headache, vertigo, tinnitus, nystagmus, diplopia, and choked disks established the diagnosis of a cerebral tumor, but no conclusion could at first be reached with regard to its location. During the year 1890, however, other symptoms developed which aided in the localization. The patient gradually became deaf in the left ear; he began to stagger in walking with a tendency to fall forward and toward the right, and a very marked tendency to turn toward the right in walking along a straight line. In addition, there developed a weakness in the right hand and exaggeration of the knee-jerk on the right side, with slight clonus in the right foot. There was no ataxia or disturbance of sensation in the limbs. The staggering was that of a drunken man, without falling, but with every appearance that the balance was quite uncertain, and the tendency to turn and fall to the right was quite constant and noticed at every examination. The pain and numbness in the left half of the face continued occasionally during the year, but there was never at any time any anesthesia. The tinnitus in the left ear disappeared gradually and the deafness in the ear increased. The headache, which at first had been frontal, was later referred more and more constantly to the left occipital region, and in speaking of it he habitually put his hand back of his ear.

A thorough course of specific treatment was carried out during the years 1890 and 1891 without any results. Toward the close of 1891 his condition had become one of complete helplessness and total blindness. The staggering was so exaggerated that he could not walk about without the help of two persons, and he was finally induced to enter Roosevelt Hospital in December, 1891, for an



operation. This operation was done by Dr. McBurney on December 3, 1891. The left half of the occipital bone was exposed by a tongue-shaped flap. The bone was removed by chisel and mallet, an opening about an inch and a half in diameter and triangular in shape being made through the occipital bone. The dura bulged strongly through this opening, indicating great increase of intracranial pressure. When the dura was divided the cerebellar tissue protruded, and it was necessary, in order to go on with the operation, to cut off quite an amount of cerebellar substance in order to palpate the parts below. The finger was introduced along the various accessible surfaces of the cerebellum, but nowhere was it possible to reach the tumor. Hemorrhage was only moderate, and easily controlled by pressure. The flaps of the dura were united, the overlying soft parts replaced and fastened with catgut sutures, the skin wound being sewed with silk.

Convalescence was perfectly satisfactory from the immediate operation, and six days after the operation, normal temperature having been maintained throughout, primary union was found throughout the whole extent of the wound, and all sutures were removed. The patient, therefore, had recovered from the operation, but the operation had been of no service. There was every reason to believe that he would have remained in the condition in which he was before the operation, but unfortunately, on the seventh day he fell out of bed, and soon after died from a hemorrhage which had occurred, as a result of this fall, under the skin flap.

At the autopsy a gliosarcoma, quite distinctly limited, from the cerebellar and adjacent tissue, was found lying on the base and compressing the left hemisphere of the cerebellum on its anterior inferior surface, pressing upon the left half of the pons and compressing the seventh and eighth nerves.

This I believe to have been the first attempt of the surgeon to remove a tumor from this cerebellar pontine angle, and the lesson to be drawn from the operation was that by a unilateral opening through the occipital bone it was almost impossible to reach the tumor. Reference to Fig. 1 will show that a great portion of the cerebellum lies between the bone at this location and the tumor. In spite of this difficulty, another attempt was made by Dr. McBurney, on March 12, 1893, to remove a similar tumor, and with success. The history of this case is as follows:<sup>4</sup>

CASE II.—*Tumor of the acoustic nerve; operation; tumor removed; death.* W. W., aged ten years, began to suffer, in October, 1892, from frontal headaches, worse at night; then from an occasional vertigo and attacks of intense headache, associated with vomiting, and occurring every third or fourth night. During December he became rather dull mentally and very irritable, and

<sup>4</sup> Reported in *Brain Surgery*, Case XXIV, p. 247, Wm. Wood & Co., 1893.

then the symptom of staggering was first noticed. During January, 1893, he was examined by Dr. Kipp, of Newark, who found a well-marked condition of optic neuritis, and then for the first time he

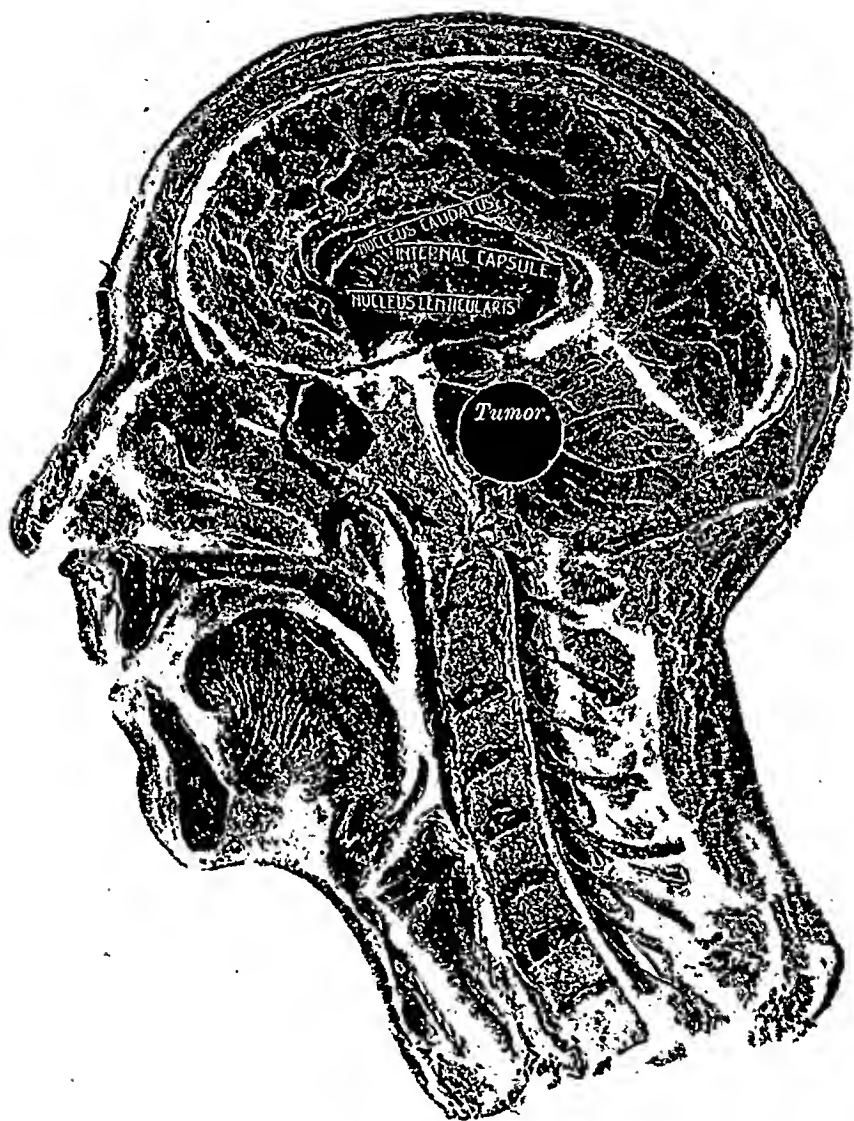


FIG. 1.—Fraser's photograph of a sagittal section of the head, showing the situation of the acoustic tumor in Cases II and VI.

noticed some dimness of vision. At that time he was still able to read large print without much difficulty, but by February 1 he had become almost totally blind. During February the headaches, usually nocturnal, increased in severity, were always associated

with vertigo and vomiting, and he began to have ringing in the left ear and deafness in the right ear. His gait was noticed to be very unsteady, his eyes were prominent and in constant oscillation, and his mental dulness was intense.

He was referred to me by Dr. William Pierson, of Orange, N. J., on March 12, 1893, with the preceding history.

Examination showed a fairly nourished but pale little boy, with a large head, prominent forehead, protruding eyes that were blind and in constant lateral oscillation. At rest, there was a manifest tendency of the right eye to turn inward, but he could look in either direction without apparent paralysis of the ocular muscles. All ocular movements were attended by marked nystagmus. Very extensive optic neuritis was found in both eyes, and he was blind. Smell was lost in the left nostril. There was no apparent paralysis or anesthesia in any part of the body or face, but a slight facial paresis on the right side was noticeable, and he was unable to whistle on account of inability to close the right half of the mouth. His hearing was decidedly defective in the right ear. His reflexes were diminished in both knees. His gait was distinctly a staggering gait, with a very marked tendency to stagger toward the left side. In groping his way forward he would tend to turn toward the left side. He described his headaches as being agonizing, and referred them entirely to the frontal region. The skull was tender to percussion over the vertex. The headache was very much increased by a recumbent posture, so that for many nights he had sat up all night.

The diagnosis of a tumor in the cerebellar pontine angle was reached by the symptoms of cerebellar gait, with a tendency to stagger to the left side, by the deafness in the right ear, and slight weakness of the right side of the face and of the right external rectus muscle, and an operation was therefore recommended.

On March 15, 1893, Dr. McBurney exposed the occipital bone on the right side, chiselling it away and enlarging the opening so far as possible in all directions by a rongeur. On dividing the dura, which bulged tremendously, a cyst, containing a dram of yellowish-green fluid, was exposed and evacuated. When the cerebellum was crowded over toward the median line beneath this cyst wall, a tumor was felt. The portion of the cerebellum which had bulged into the wound was then sliced off in order to give access to this tumor. It was gradually enucleated by the aid of a finger and a spoon. It contained one or two small cysts, which ruptured in the process of its extraction. It was gradually removed, being shelled out from the cavity in the cerebellum; it had no distinct capsule. Clean cerebellar tissue was left around the previous site of the tumor. Hemorrhage was arrested by compression and by packing the wound, and a drain was left in the wound, and the dura and scalp were closed.

The boy recovered from the shock of the operation, but gradually grew weaker, and after about two weeks died in the hospital. This was, I believe, the first successful case of removal of a tumor from this locality.

The record of operations upon the cerebellum up to the close of 1893<sup>5</sup> showed that 15 cases had been operated upon, and that in one only had successful removal of the tumor, with recovery of the patient, been recorded. Discouraged by this record, for a number of years I refused to recommend operation in cases of cerebellar tumor.

The next case I will not give fully. It was one in which the autopsy showed a cyst of the cerebellar pontine angle. The most prominent symptom was a mental deterioration and progressive dementia. No diagnosis of the location was made.

CASE III.—*Cyst of the cerebellar pontine angle; no diagnosis; autopsy.* Female, aged fifty-three years, began to suffer in October, 1895, rather suddenly, from a numbness of the entire left side of the body and marked unsteadiness in gait. Soon after she noticed that the leg felt heavy in walking, so that she thought she dragged it, but as a matter of fact she used all the muscles freely. During this time the motions of her left hand became awkward, and it was found that she frequently let things fall out of her hand. During the winter of 1896 these symptoms continued and increased, and it was noticed that she was becoming progressively more and more dull mentally, as shown by her lack of interest in things about her when sitting idle, when formerly she had been an active woman, and by her becoming unable to play whist.

When seen on January 24, 1896, in consultation with Dr. Adler, her optic disks were found to be normal; fields of vision normal; ocular movements normal, but attended by a nystagmus on turning the eyes to either side. There was a flatness of the left side of the face, the left eye not winking normally with the other, but it was possible to close the eye, and voluntary movements of the lips and cheek were perfect. There was no paralysis of the left arm or leg, motions of resistance in all directions and in all muscles being perfect and reflexes normal, but there was a marked ataxia of both left arm and hand and of the left leg. The hand was held in an awkward position. Her sense of position of the hand in space and of the position of the fingers was imperfect, but sensations of touch, temperature, and pain were normal and equal on both sides. She had complained of a good deal of pain over the left ear and behind the left ear, but she had no deafness, no vertigo, no vomiting. The case, therefore, at this time seemed to be quite obscure, and no diagnosis was possible. She was subject to uterine hemorrhages, and was exceedingly anemic, and for this condition she was treated

<sup>5</sup> Brain Surgery, p. 249.

during the year of 1896, but during that year she became progressively worse, the feebleness of the left side and awkwardness steadily increased, so that by October, 1896, she was unable to walk without help, and in November, 1896, she was confined to her bed. The ataxia of the arm had also increased during this time, so that the arm was practically useless for finger movements; she could no longer feed herself or adjust her hair. The facial paralysis on the left side had also increased.

When seen again, on January 17, 1897, in consultation with Dr. Polk and Dr. Knapp, the facial paralysis was quite complete, of the peripheral type. The power in the left arm and left leg was almost normal, but the ataxia in both limbs was very pronounced. Motions of the eyes produced nystagmus, and it seemed impossible for her to turn her eyes conjugately toward the left, but there was no strabismus. During the year of 1896 her mind had become progressively impaired, so that in January, 1897, she was almost in a condition of stupor. It was with great difficulty that she answered any question. She did not seem to pay attention to questions or to requests until they had been repeated over and over, but then, when they finally appeared to reach her consciousness, she would answer or act appropriately. She could not balance herself in a sitting posture in bed; she had been totally incapable of standing on her feet for a month or more, and if held up in the bed her head fell backward, and a great deal of pressure backward was made of the entire body. This tendency to fall backward had been noticed by others for several weeks. For the last two months there had been an absolute lack of control of the sphincters, and she had paid no attention to the wants of nature. This was ascribed to the obscure mental condition. The optic disks, examined by Dr. Herman Knapp, were found to be normal. There was apparently no deafness, no anesthesia, no blindness. She did not suffer from headache, vertigo, or vomiting; she was fairly nourished.

During the month of January she lay in the same condition of stuporous indifference to her surroundings, never roused up of her own accord, or spoke, though if sharply questioned, after a considerable length of time would reply accurately. In addition to the facial paralysis of the left side, there had developed by February 1 an anesthesia of the left cornea and slight tactile anesthesia of the left side of the face. The tendon reflexes of the left side had become much exaggerated, the ataxia remained, but no paralysis had appeared. During the month of February she grew progressively more feeble, an infection of the bladder occurred, and on March 2 she died.

The autopsy showed the existence of a cystic tumor lying on the left side of the pons, at the position of its junction with the medulla and the cerebellum, all of which organs were deeply indented by the tumor. The tumor measured 5.5 cm. in an anteroposterior

direction, 4.5 cm. laterally, and 2 cm. vertically. It was a cyst filled with fluid of a whitish color, in the walls of which irregular thickenings of fibrous nature were seen. The tumor was not adherent anywhere to the brain, but it was adherent to the dura just behind the ridge of the petrous portion of the temporal bone. The seventh and eighth nerves ran in the wall of the tumor, and were torn off from the brain in removing it. The sixth nerve had been compressed by the anterior edge of the tumor. The pressure of the tumor had indented the pons deeply upon its side, but had not compressed the pyramidal tracts of the medulla. The pressure on the medulla had been exerted upon the olivary body and restiform body, which were compressed backward. The cerebellum was deeply indented in its middle peduncle, so that when the tumor was removed a deep indentation in the middle peduncle of the cerebellum was visible. The ventricles of the brain contained a considerable amount of clear serum, and were distended more in the posterior horns than in the anterior, but this distention was not very marked. The brain did not appear to be very much compressed, the convolutions were not markedly softened, and the dura was not very tense. There were no changes in the pia and no hemorrhages within or upon the brain. The cerebral hemispheres were normal.

In reviewing the history of this case, which was throughout its clinical course most obscure, and in which the only general diagnosis was one of brain tumor without any definite localization, it is evident that the pressure upon the seventh nerve was the first symptom, together with the ataxia of the limbs on the side of the tumor, with a tendency to fall in walking, to stagger, and to fall backward. As the tumor advanced, the left sixth and fifth nerves were involved, but it is rather surprising, in consideration of the fact that the tumor involved the acoustic nerve, that there were no symptoms of deafness or of vertigo, and in view of the size of the tumor, it is quite surprising that there were no symptoms of optic neuritis. The mental condition was really the most noticeable of all the symptoms present.

While mental symptoms occur in between 50 and 60 per cent. of all cases of brain tumor, as shown by the careful analysis made by Schuster,<sup>6</sup> yet it has been noticed that in tumors of the cerebellum such mental symptoms are only present in about 25 per cent. of the cases. As a rule, they consist of a progressive stuporous condition, with dementia; rarely hallucinations occur; usually there is a condition of progressive inability to use the mind. I have elsewhere pointed out the frequency of this symptom in connection with tumors of the corpus callosum and of the frontal lobes.<sup>7</sup> But the

<sup>6</sup> *Psychische Störungen bei Gehirn Tumoren*, Stuttgart, 1902.

<sup>7</sup> *AMER. JOUR. MED. SCI.*, 1895, "Tumor of the Corpus Callosum, with Autopsy," by Francis and Starr.

case here put on record is the only case of tumor of the cerebellum which I have seen in which such mental symptoms appeared. Ballance<sup>8</sup> states that the mental state is normal, or only affected late, as a consecutive phenomenon. Glasow,<sup>9</sup> in recording a case of cerebellar tumor, has noticed such mental symptoms, but the rarity with which these symptoms are recorded in the large number of cases of cerebellar tumor which I have been able to gather convinces me that the percentage given by Schuster is excessive, and than in not more than 10 per cent. of cerebellar tumors are mental symptoms observed in the early stages. It is, of course, true that in the later stage of the disease, when the ventricles are distended by fluid and the general intracranial pressure is much increased, under which circumstances the patients are likely to be blind, a demented state may develop, but as an early symptom of tumor of the cerebellum, I believe mental disturbances are most unusual.

In 1903 the following case was seen at the clinic, and was sent to the Presbyterian Hospital for the purpose of an attempt at removal of the tumor.<sup>10</sup>

CASE IV.—*Tumor of the acoustic nerve; sudden death.* F. K., aged seventeen years, when seen at the clinic, had all the symptoms of brain tumor, which had lasted about a year, developing gradually. She had severe headaches, worse in the morning on awakening; attacks of vomiting; intense vertigo, and double choked disk, which was gradually impairing her eyesight. She had also a typical cerebellar ataxia, staggered in walking, found it difficult to maintain her balance, and had a marked tendency to stagger toward the right side.

Examination showed a slight weakness of the left external rectus muscle, flattening of the left side of the face without any actual paresis, and marked deafness in the left ear. While there was no paresis of the limbs of the right side, the reflexes on that side were markedly exaggerated. She had had many attacks of sudden faintness with vertigo and a sensation of alarm, which were interpreted as vagal attacks. She had become somewhat dull mentally, but was intelligent enough to give satisfactory answers to all questions, and presented no other symptoms than those here described.

It seemed probable from these symptoms that the tumor lay upon the base of the brain, involving the cerebellum, the sixth, seventh, and eighth cranial nerves, and with this diagnosis in view, Dr. McCosh agreed to operate and attempt to remove the tumor. While the patient was being examined by the house surgeon, on the day prior to the date fixed for operation, she suddenly fell back in bed, became cyanotic, and ceased to breathe. Artificial respiration was immediately begun, and so long as it was kept up the cyanosis

<sup>8</sup> Some Points on the Surgery of the Brain, p. 232, Macmillan Co., 1907.

<sup>9</sup> Archiv f. Psychiatrie, xlv. 310, Berlin, "Zur Kasuistik der Gehirnn Geschwülste."

<sup>10</sup> See Brain Surgery, p. 253.

was relieved, her pulse beating normally though rapidly. She was, however, completely unconscious. Artificial respiration was kept up in this manner for eight hours, all possible means of resuscitation were tried, but no natural respiration appeared to be possible, and although her heart continued to beat after respiration was suspended, it seemed impossible to prolong her life, and at the end of eight hours she died.

No autopsy was permitted in this case, but recent investigations have shown that the cause of death in such cases is the pressure of the tumor above forcing cerebellar tissue downward into the foramen magnum and thus compressing the respiratory centre.<sup>11</sup> It seems reasonable to suppose that this occurred in this patient. The condition found in the case soon to be described (Case VI) warrants this supposition.

Bernhardt<sup>12</sup> called attention to the greater frequency of sudden death in cases of tumor of the cerebellum than in tumors elsewhere in the brain, his statistics showing the ratio as 24 per cent. to 7 per cent.; and both Oppenheim and Bruns confirm this observation. Horsley<sup>13</sup> recorded 3 cases of sudden death in his record of 95 cases of brain tumor. Tietze<sup>14</sup> reported a sudden death after lumbar puncture, and Cushing<sup>15</sup> has called particular attention to the risk of lumbar puncture in cases of cerebellar tumor, and has recorded two fatal cases and one case in which life was saved by prompt operation after respiration had ceased.

In the following case the diagnosis of a cerebellar tumor was comparatively easy, but the result of the operation was not favorable:

CASE V.—*Glioma of the cerebellum, invading the pons; operation; death.* L. B., aged seven years, was sent to me by Dr. Francis, of Montclair, on September 30, 1904. Her symptoms had gradually developed during two years prior to this time, following a blow upon the head on the left side in the parietal region, where there existed a marked thickening of the bone. Headache, vomiting, and optic neuritis had developed slowly, with a progressive diminution of her mental development, and after a year of these symptoms ataxia in her gait was noticed, together with an awkwardness of the arms, most marked upon the right side. The ataxia of gait increased steadily during the second year, so that when she was examined it was very difficult for her to walk, and in consequence of the inactivity of the right side, there was a marked atrophy of both arm and leg, considerable weakness in them, and a slight disturbance of sensation felt as a numbness.

<sup>11</sup> For a photograph of this condition see Turner and Stewart, Text-book of Nervous Diseases, p. 236.

<sup>12</sup> Beiträge zur Diagnostik der Hirngeschülste, Berlin, 1881.

<sup>13</sup> Brit. Med. Jour., August 23, 1906.

<sup>14</sup> Berlin. klin. Wochenschr., May 18, 1908.

<sup>15</sup> Interstate Med. Jour., September, 1909.



During the year prior to the date of examination she had had four attacks of stupor, each lasting several days. They were usually preceded by vomiting and attended by high temperature, and on each occasion the child's life was despaired of, as it was impossible to feed her, and the bladder and rectum were not under control. After each of these attacks, however, she gradually recovered consciousness, and seemed a little better after each attack than she had been before it.

When examined, she was found to have double choked disks and to be almost completely blind. She had exophthalmos of the right eyeball and paralysis of the right external rectus muscle. She had a flattening of the right side of the face, a loss of corneal reflex, slight anesthesia of the right side of the face, and some deafness in the right ear. She could not sit up or hold her head up, and when held up it tended to fall forward. She had a very marked ataxia of the right hand and of the right leg, some ataxia also in the left hand. No absolute paralysis in any muscle. No history of convulsions, of vertigo, of insomnia, of change of pulse. A course of mercury and iodide of potassium had been carried out with marked improvement for a few months, but was followed by a relapse.

The diagnosis in this case was a tumor in the right half of the cerebellum on the base, compressing the sixth, seventh, and eighth cranial nerves on the right side, and producing the ataxia of the right limbs due to injury of the cerebellum on the right side; and an operation was at once recommended. This operation was done by Dr. McCosh on November 15, 1904, at the Presbyterian Hospital. The occipital bone was exposed over the right side, but when the periosteum was stripped back venous hemorrhage occurred in an alarming condition from the bone, which appeared to be soft and porous, and which was controlled only by packing and pressure. This packing was removed on the second day, but the bleeding recurred, so that further opening of the skull was not deemed possible. At this time a tube of radium was inserted into the wound and left in for half an hour, and following this each day for five days the back of the head was exposed to the x-rays for ten minutes.

The child was then sent home, as an operation was thought to be impossible, but as the symptoms, which had at first been relieved, possibly by the bleeding, recurred, and as her condition was very serious, a second operation was undertaken on December 31.

The cerebellum was exposed, and on this occasion bleeding was not severe. Exploration with the finger and with a needle failed to expose the tumor, probably on account of lack of room, the exposure having been unilateral only. The wound was then enlarged upward, the tip of the occipital lobe was exposed, a needle was introduced into the posterior horn of the lateral ventricle, a large amount of fluid was evacuated from the ventricle, and horse-

hair drains were introduced through the aspirating needle and the needle was withdrawn, thus draining the lateral ventricle. During the following three weeks this drainage was kept up; at times as much as 20 ounces of cerebrospinal fluid drained into the wound. The evacuation of the ventricular effusion was attended by very marked relief, the child became bright and active mentally, the headache disappeared, and the congestion of the veins in the retina was considerably relieved, although her sight was not improved. At the end of that time, however, the child died.

The autopsy revealed the existence of a sarcoma, occupying the right lobe of the cerebellum, infiltrating this lobe, and reaching the base upon the right side, where it had pushed the medulla over toward the left side. A small projection of the tumor ran forward upon the pons Varolii and compressed the sixth, seventh, and eighth nerves at this point. The tumor also infiltrated the middle lobe of the cerebellum, so that it lay upon and compressed the floor of the fourth ventricle. It had no capsule, and it would have been very difficult to have removed it, had it been revealed at the operation, without removal of the hemisphere of the cerebellum. The ventricles were enormously distended, and contained 455 c.c. of serum.

In this case, even had a larger exposure of the cerebellum been made, it is evident that the operation would not have been successful, on account of the infiltrating character of the tumor. The futility of x-ray and of radium treatment in a glioma is demonstrated by the result of this case.

The last case to be recorded had, however, a much more favorable result.

CASE VI.—*Tumor of the cerebellar pontine angle successfully removed, with perfect recovery of the patient.* Female, aged forty years, was referred to me in October, 1908, by Dr. Synnott, of Montclair, N. J., and Dr. Broughton, of New York, with a history of gradually advancing brain tumor. She dated her symptoms from May, 1908, but there is reason to believe that they began much farther back in her history. Occasional sensations of vertigo had been felt at intervals since 1902. A severe attack of pain in the left suboccipital region lasting two weeks, which made riding in a carriage or jolting unbearable, had occurred in 1905, but had not recurred. While pregnant, in November, 1907, she suffered much from ringing in the left ear, and noises like the sound of a sea shell or the escape of steam; also from sudden faint feelings in the stomach. She miscarried in December, 1907, and then these symptoms ceased. From May, 1908, she had been suffering from headaches, especially severe in the morning on awakening, or on awakening from sleep if she slept in the daytime, headaches that were very markedly relieved by taking food, and that seemed to have had no definite location, but to have been felt all over the head,

sometimes in front, sometimes at the back, and in the eyes. During the summer this headache was attended by a certain amount of deafness in the left ear and a slight flattening of the left side of the face, and with weakness of the orbicularis palpebrarum, so that in the act of winking it was noticed that she winked less forcibly with the left eye. During the summer considerable awkwardness of gait gradually developed, with a marked tendency to stagger in walking, and a feeling of falling, and by October this cerebellar staggering was very marked, so that she had to be supported in walking. During August she began to notice some disturbance of her eyesight, and it was this that led, in October, to her consulting Dr. Broughton, who discovered a double optic neuritis, a marked lateral nystagmus on motion to both sides, and a very marked prominence of both her eyeballs, with tendency of the eyeballs to diverge at rest. She had at that time no hemianesthesia and no paresis of the limbs, but the knee-jerks were markedly exaggerated.

The diagnosis was made of a tumor in the auditory region on the base, and the suggestion was made that she be treated with mercury and iodide of potassium, although there was no history of specific disease. Improvement in the symptoms began soon after this treatment was commenced, and for two months, November and December, she was practically free from her headache and her deafness was less marked, and her eyesight did not grow worse. In January, however, she began to suffer again from the same symptoms, gradually grew worse during February, and when I saw her on March 27, 1909, all her symptoms were more pronounced than at the first examination. Her headaches were very intense, so much so as to incapacitate her from all effort. They were worse at night and very much worse on awaking from sleep. She had vomited occasionally when the headache was very intense. They were still relieved by taking food, and she appeared to have an abnormal appetite, for she had gotten into the habit of taking food every two hours, which she seemed to digest well. But in spite of this, she had lost weight, she looked thin, and had the appearance of a person who was ill and in suffering. Her optic disks were much more swollen than they had been in October, her vision was reduced to  $\frac{2}{60}$  in each eye, and there was a marked diminution of the visual field for colors. Vertigo was a constant symptom, but it did not appear to be a vertigo in any particular direction. The deafness in the left ear had increased so that a watch was no longer heard at the ear, and bone conduction was markedly diminished to the tuning-fork. Nystagmus was very evident on any motion of the eyes, but was distinctly worse when the eyes were turned to the left. Deviation of the eyes outward was still noticed, and a very marked exophthalmos, a little more marked in the left eye than in the right. The weakness of the left side of the face was pronounced, winking being imperfect, and a

forcible closure of the left eye being impossible. Her knee-jerks were both exaggerated equally. She had begun to have some tingling and numbness in the left leg. In walking, she staggered more than she had before, and her staggering was now distinctly toward the right side. This was not due to any weakness of the right leg, which, on being tested, was found to be as strong as the other. She felt as if she were falling toward the right side when standing, and she swayed more toward the right side with her eyes closed.

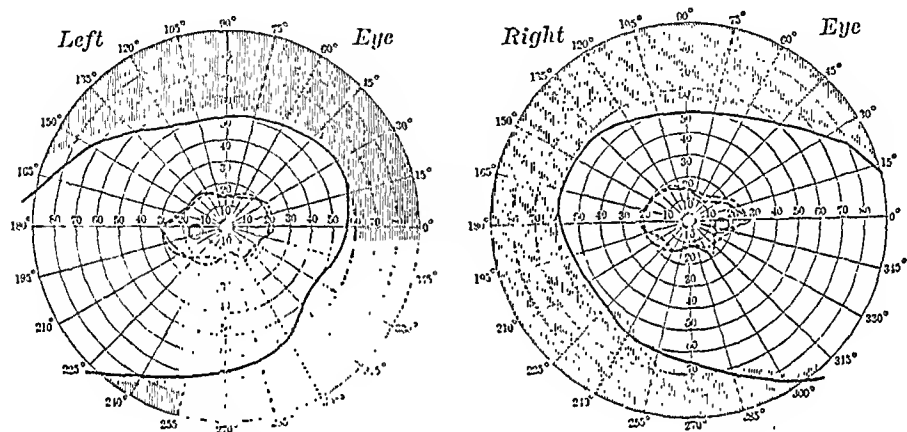


FIG. 2.—The visual fields prior to operation, showing contraction of the color fields, and interlacing of blue and red fields, with marked inversion of the fields. (Dr. Bordley.) (. . . . red; —.—.— blue.)

The failure of the constitutional treatment to have any effect in relieving her permanently led me to advise an operation, and knowing the success which Dr. Harvey Cushing, of Johns Hopkins, Baltimore, had had in such cases, I suggested that she go to him for operation. After some delay this was agreed upon, and she went to Baltimore on May 14.

Examination in Baltimore at that time confirmed the existence of the symptoms here recorded, and, in addition, very careful perimetric measurements of the visual fields were made, which are here given. These showed a diminution of the visual fields of color, with an interlacing of the red and blue fields, as shown in the diagram, a condition which Drs. Bordley and Cushing have pointed out as a valuable symptom of brain tumor. The swelling of the optic disks was 5 D. At that time, before the operation, she was also suffering from numbness in the leg, arm, and face on the left side. She had a great deal of ringing in her left ear, associated with the deafness; she had marked double vision; she had a sensation of falling, especially toward the right side, and it was found that on lying on her back or on either side in bed, or on changing her position in bed, the sensation of vertigo was very markedly increased.

She could not lie at all on her left side. It was also discovered that in rapid motions of the hands some awkwardness was apparent in the left hand. This did not amount to any disability, as she could feed herself and fix her hair perfectly, but on simultaneous rapid motions of the fingers and wrist it was evident that the left hand presented a certain degree of incoördination. The staggering toward the right was particularly noticed. In obtaining her history Dr. Cushing elicited the fact that for a number of years she had been somewhat unsteady on her feet in certain movements. Thus, as far back as 1900 she had noticed in playing golf that she felt very unsteady when addressing the ball in sending it off, and that it had become practically impossible for her, in 1905-06 to play golf with her accustomed facility, because of the difficulty in maintaining her balance and hitting the ball accurately, so that in 1906 she had given up playing golf entirely.

It seems probable, therefore, that the symptoms had begun with a slight degree of imperfect balance eight years before the occurrence of the headache, which was considered the first symptom of the tumor, a fact which indicates that in all cases of brain tumor it is wise to ascertain whether little unusual manifestations of activity, sensation, speech, or conduct may not have preceded the active development of the symptoms by some years.

Another symptom elicited by Dr. Cushing was the occurrence occasionally during the two years prior to the development of the headache of peculiar attacks, known as vagal attacks—a sudden sensation of alarm and faintness without an actual faint, attended by palpitation of the heart and probably by a very rapid pulse—an indication of irritation of the vagus nerve or nucleus from pressure of the medulla. The patient had not thought it worth while to mention these symptoms, but when questioned, had a distinct remembrance of having had numerous such attacks for two years.

Dr. Cushing concurred in the diagnosis of a tumor in the cerebellar pontine angle, and on May 20 performed a successful operation.

The patient was laid upon the table, face downward, the body being supported by pads beneath the shoulders, which were adjusted before the anesthetic was given, and the head was supported by a special crutch adjusted to the forehead, not attached to the table, and after she was comfortably arranged the anesthetic was administered by a physician sitting beneath the table. A bow-shaped incision was made across the occiput and extended over on both sides to the ear, and a vertical incision in the median line was made downward from the middle of this bow-shaped cut. In this way two triangular flaps were made downward and outward, as indicated in Fig. 3. When the occipital bone in its entire surface had been exposed, small trephining openings were made on each side, and the opening was then enlarged by rongeur forceps until all of

the central part of the occipital bone had been removed. The median ridge between these two openings was then rongeured away and the bone was taken away down to the foramen magnum. The posterior third of the bone forming the foramen magnum was also removed, it being evident that the brain within the dura was pressing downward into this foramen. When the occipital bone was thus entirely taken away and the foramen had been opened, it was evident that the intracranial pressure had abnormally increased, as the dura bulged markedly from the opening made, and when the dura was opened the compression of the cerebellar tissue beneath



FIG. 3.—Showing field of operation eighteen days after it.

it was manifest not only by the bulging, but by the existence of a marked ridge upon the cerebellar tissue, showing the pressure that had been exerted along the edge of the foramen magnum, and the cerebellar tissue had evidently been forced downward into the foramen at least three-quarters of an inch below its upper level. This appearance of the cerebellum, having been forced downward into the spinal canal, confirms the statement made of the existence of such pressure, and of the possibility of such pressure producing sudden death by compression of the medulla. It is undoubtedly a fact that this patient would have died suddenly had this operation not been performed, and it is hardly conceivable that such a fatal

termination could have been postponed very long in consideration of the enormous amount of pressure evident from the cerebellum.

When the margin of the cerebellum was lifted and the pia was incised, a large amount of fluid escaped, and then the cerebellum fell back into its normal position.

By careful manipulation and raising the cerebellar hemisphere upon the left side and pushing the entire organ over to the right side, access, little by little, was obtained to the deeper structures. The difficulty experienced in previous operations (Cases I and II) of obtaining access to the base of the brain was obviated in this case

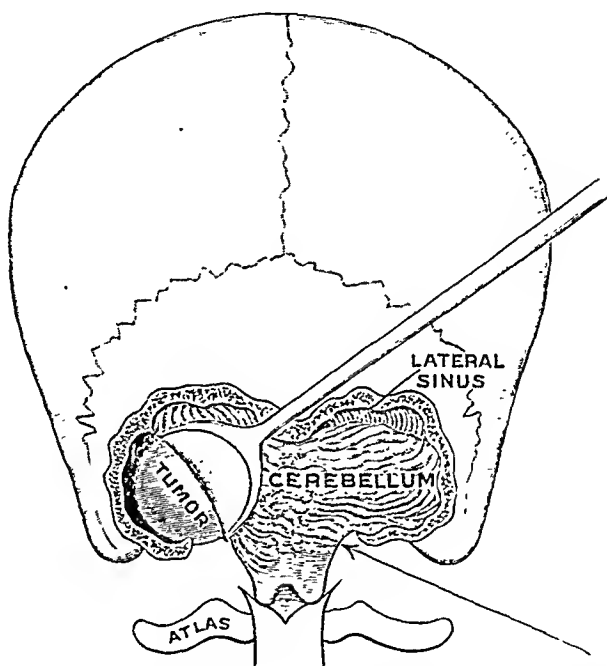


FIG. 4.—Sketch of operation by Dr. Harvey Cushing. The arrow points to the level of the foramen magnum showing the foraminal herniation of the cerebellum.

by the possibility of displacing the cerebellum over to the right side, because of the removal of the right half of the occipital bone. Had but one-half of the occipital bone been removed, it would have been impossible to have exposed the deeper structures or to have reached the tumor. When the cerebellum was elevated sufficiently a white, hard mass was discovered by the finger and soon came into view, the wound being illuminated by a powerful electric lamp attached to the operator's head (Fig. 4). This tumor was evidently encapsulated, was not attached to the surrounding structures excepting by a small pedicle at its base; by careful manipulation with the finger and a spoon it was enucleated, its pedicle severed, and it was removed with a very little hemorrhage. Such hemorrhage as there was, was arrested by packing with cotton wet with

adrenalin solution. The removal of the tumor enabled the operator to have space enough to return the cerebellar tissue easily within the dura. The cavity left by removal of the tumor was filled by a sterile salt solution. There had been no laceration of the cerebellum attendant upon the operation. The dura was closed, the scalp sewed with silk sutures, and although the operation had occupied more than two hours, the patient had no perceptible shock, and on recovering from the anesthetic, was found to be very comfortable. She made a steady progress to recovery. Fig. 3 shows the condition of the scalp at the site of the wound eighteen days after operation.

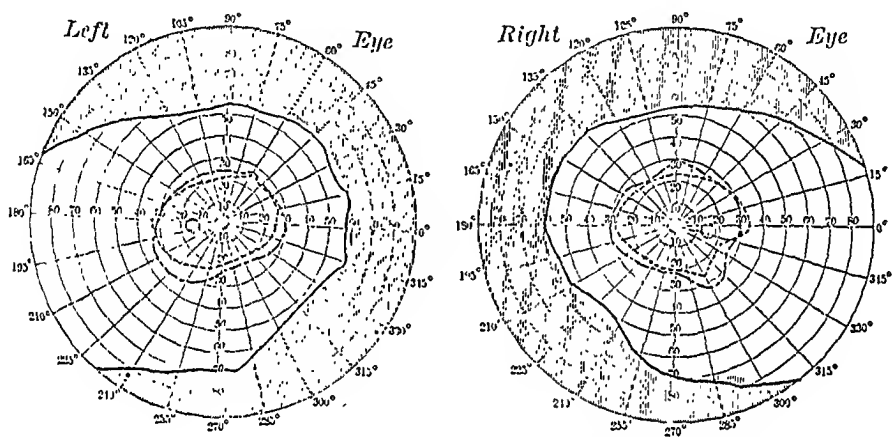


FIG. 5.—Visual fields one month after operation: very slight inversion persists; the blue field is generally larger than the red. (Dr. Bordley.)

Careful examination on June 18, one month after the operation, by Dr. Cushing, elicited the following facts: There was no sign of headache; there was a complete disappearance of numbness in the leg, arm, and face; there was no ringing in the ear; there was a marked subjective improvement in vision, and the visual fields showed a regaining of the normal contour, both for white and for color, a marked enlargement of the visual field for color being evident. The disks were reduced to 1.5 D. She was able to walk more steadily than for many months, but still felt a certain uncertainty in her gait, but had no tendency to stagger to one side. Her old discomforts associated with a change of position had disappeared. She was now able to lie on her back or on either side in bed. She had no longer any sensation of falling; the diminished acuity of hearing in the left ear to air conduction had practically gone, although there was a slight deafness still to bone conduction; the awkwardness in the left hand had disappeared. The only remaining evidence of the old lesion was the nystagmus of the eyes and the increased knee-jerks.



The appearance of the tumor is shown in Fig. 6, together with measurements in centimeters. The size of the tumor is 2.5 cm. in two of its diameters, and 2 cm. in the third diameter. It is a hard, white, encapsulated tumor, presenting the appearance of a fibroma, and was found to be, on microscopic examination, a pure endothelioma.

The examination of this patient, on February 5, 1910, shows a state of almost perfect health. She has no choked disks, the retinae appear to be normal, her visual field is perfect for light and for color, and there is no congestion of the veins of the retina. She walks perfectly well, without any tendency to stagger, and has no vertigo. She has had no headaches during the summer. She has no anesthesia or weakness of any part of the face or body.



FIG. 6.—Endothelioma of acoustic nerve (centimeter measure)

She has nystagmus on lateral motion of both eyes, a slight deafness to the tuning-fork and to air conduction in the left ear, and exaggeration of both knee-jerks, but no ankle clonus, and she feels perfectly well. She goes about New York alone, her hair has grown naturally over the wound, and there is no tenderness of the scalp. The marked exophthalmos which was present has gradually subsided, so that there is no trace of it at present, and her winking is symmetrical on both sides.

The interest of this case lies, first, in the possibility of an accurate localization of the tumor, as shown by the analysis of the symptoms; second, in the possibility of successful removal when a sufficient field of operation is obtained by an extensive removal of bone; and third, in the fact that when such a tumor, lying upon the brain without destroying the brain tissue, is removed, a complete recovery of function in the brain tissue previously compressed is quite possible.

OPERATIONS FOR TUMORS OF THE CEREBELLUM AND ACOUSTIC NERVE. In the early days of cerebral surgery the results of cerebellar operations were so unfavorable as to make surgeons unwilling to undertake this operation, but as greater care and skill were developed, and the technique was improved, successful cases were more frequently recorded, so that, year by year, the percentage of recoveries increased. In 1905 Frazier was able to collect the records of 116 cases of cerebellar tumor in which an operation had been undertaken. In 52 cases the tumor had been found at the operation; in 34 cases it had been removed successfully, and in 17 cases recovery from the operation and from many of the symptoms which had been present prior to the operation had occurred. I have been able to collect from the literature between January 1, 1905, and January 1, 1910, 128 cases in which an operation had been undertaken, in which the tumor has been found and in which it has been removed (the tables of these cases are appended). I have not included in these tables cases in which an operation has been undertaken but in which no tumor was found, although there are nearly 50 such cases of failure recorded in the literature in the last five years. The analysis of these tables shows:

	Cases.
Tumors of the cerebellum removed, with recovery of patient . . . . .	76
Tumors of the cerebellum removed, with death of patient . . . . .	52

Constructing a table from the combination of statistics of Frazier and myself up to January 1, 1910:

	Cases.
Total number of operations for cerebellar tumor . . . . .	294
Tumors found and removed . . . . .	162
Recovery of the patient from operation and from symptoms . . . . .	69

By the term recovery it is intended to imply not merely survival of the patient after the operation for a few days, but relief from the symptoms present in greater or less degree for a period exceeding three months. It is true that some of these patients remain with imperfect sight or hearing, and that some have remained somewhat ataxic in their gait, or with partial paralysis of some one of the cranial nerves. On the other hand, a number have been reported as completely recovered after several months, or even years, one case of Ballance having survived the operation already twelve years when the report was made.<sup>10</sup> In the case described in this article I see every reason to believe that the patient is permanently well, as she shows few, if any, symptoms at the end of ten months.

Such results certainly justify the operation, and make it evident that, as experience grows and technique is perfected, the many

<sup>10</sup> Ballance, *Some Points on the Surgery of the Brain*, p. 281.

dangers of the operation will be overcome, the operation will be undertaken earlier, and the percentage of recoveries will steadily increase.

*The Method of Operation.* A study of the various methods recommended by Horsley, Ballance, Borchardt, Krause, Biro, Frazier, and Cushing has convinced me of several important facts:

1. The necessity of a large exposure of the cerebellum by a bilateral operation, exposing and removing the entire occipital bone. Such an operation is long and difficult, the hemorrhage from the soft tissues and muscles of the neck is liable to be excessive, and in many instances an exposure of the occipital bone reveals foramina in that bone traversed by veins, giving the bone a cribiform appearance, which give rise to very severe hemorrhage. Thus, in a case of cerebellar tumor operated upon for me by Dr. McCosh, in 1900,<sup>17</sup> it was absolutely necessary to stop the operation on the exposure of the occipital bone, to plug the sinuses which were open with wax and with ivory points, and to give up any idea of further procedure, arresting the hemorrhage by bandages, the removal of which on the second day was followed by such a considerable degree of hemorrhage that any further attempt at removal of the bone was abandoned. The blood flowed through the foramina in the occipital bone in continuous stream, as if from a sinus, and the bone, which had been probably somewhat thinned by the pressure of the tumor within, bled freely wherever it was touched with an instrument. Others have found the same difficulty, but in cases of hemorrhage it is sometimes possible to arrest the hemorrhage by insertion of Horsley's wax into the bleeding foramina, or by plugging small openings with bone points or with wooden plugs.

2. A bilateral operation, removing the bone from both sides of the cerebellum, and then removing carefully the intermediate ridge of bone lying vertically between the two halves of the cerebellum over the occipital sinus, is necessary in order to give proper space for the displacement of the cerebellum to one side or the other during the operation, so that access may be had to the deeper parts in cases in which the tumor lies in the pontine angle. When only one side of the occipital bone is removed, the space opened is rarely more than two inches in diameter. Through this opening the cerebellum bulges greatly when there is a tumor within it or beneath it, and thus the cerebellar tissue stands in the way of any access to the deeper parts. In one case operated upon by Dr. McCosh,<sup>18</sup> under these circumstances, about one-half of the cerebellar hemisphere was sliced away and removed, much of it having become bruised and lacerated through bulging outward and by the necessary manipulations. This loss of cerebellum did not appear

<sup>17</sup> This case is not included in those already cited—Case V in my table.

<sup>18</sup> This case is not included in the cases here cited. Case VII.

to have any ill effects subsequently upon the patient. Horsley has recorded a similar case,<sup>19</sup> in which a considerable part of the cerebellar hemisphere was destroyed in an operation without any ill effects. Hartley<sup>20</sup> also records a case in which a half of the cerebellar lobe was removed in an operation for the removal of a cerebellar tumor, where no tumor was found, but a decompression only was accomplished, in which case the patient recovered perfectly, and was well three years later, without any symptoms referable to a loss of one-half of the cerebellar lobe. While it appears, therefore, that a destruction of cerebellar tissue may be survived without any permanent ill effects, even to the extent of one-half of a cerebellar hemisphere, yet such a destruction of the cerebellum may be avoided by a bilateral exposure.

3. One of the dangers attendant upon this operation, and one which has led to sudden death during or immediately after the operation, is traction upon or pressure upon the vital centres in the medulla oblongata during the operation. If plenty of space is obtained for the displacement of the cerebellum to the side away from the tumor, by a large exposure, such pressure and traction may be avoided. It seems, therefore, incumbent upon the operators to expose the entire cerebellum before attempting to extract the tumor.

4. Inasmuch as this exposure is a difficult matter, involving considerable hemorrhage and taking a long time, it seems advisable that this operation should be completed and the removal of the tumor attempted at a second operation, to be done from five to ten days after the first. In this way shock, which is the second chief danger in these operations, may be avoided. Furthermore, the removal of the occipital bone relieves the intracranial pressure at once, and in some cases in which the tumor subsequently was not found, this decompression in itself has been sufficient to cause great improvement in the symptoms. Thus, I desire to put on record here the history of a case of a young man sent to us from Charleston, S. C., the son of a physician, who was operated upon by Dr. McCosh, in the Presbyterian Hospital, in 1902.

CASE VII.—*Probable cerebellar tumor; decompression; recovery.* This young man presented all the general symptoms of tumor—headache, vertigo, vomiting, and optic neuritis—together with marked cerebellar ataxia and tendency to stagger backward, but without any symptoms referable to the cranial nerves or to the tracts passing through the pons and medulla. The tumor was, therefore, thought to be in the middle lobe of the cerebellum and beneath the tentorium, and not near the base.

In this case both halves of the cerebellum were exposed by a free removal of the occipital bone, but no tumor was to be found

<sup>19</sup> Brit. Med. Jour., August 23, 1906.

<sup>20</sup> Annals of Surgery, xlv, 518.

after careful exploration with the finger and with an aspirating needle in all directions. The operation, which was followed by immediate surgical recovery, was succeeded by a general progressive improvement, the choked disk gradually subsiding, though the sight did not improve materially, as permanent damage had been done to the optic nerves, but his headache, vomiting, and vertigo were relieved, his ataxia disappeared, and he went home at the end of two months fairly well, and has been heard of at intervals since, having been apparently entirely relieved from his symptoms, excepting for a moderate degree of blindness. The last report was four years after the operation.

Similar cases have been recorded by Cushing<sup>21</sup> and by other operators, and in Frazier's statistics 13 per cent. of the patients were improved by the operation, even when the tumor was not removed. The relief of pressure, therefore, at the first operation, is likely to improve rather than to hurt the patient.

5. In the second operation, or the second stage of the operation, the first step is to prevent hemorrhage from the occipital sinuses, by tying them with an aneurism needle and double suture before the dura is divided. Then a transverse incision, curved upward, is to be carried from one side across to the other, allowing the dura to be reflected downward, so as to give a thorough exposure of the cerebellum. It is most important that in the removal of the occipital bone the posterior edge of the foramen magnum should also be removed. In a large number of the cases of cerebellar tumor a portion of the cerebellum is wedged down into the spinal canal. If the posterior portion of the foramen is removed, the cerebellum can easily be loosened and turned upward without undue traction. When the dura is divided the cerebellum may be lifted upon the spatula, and exploration of the cerebellar pontine angle may thus be made. In this procedure the cerebellum has to be pushed over to the opposite side, and anyone who has watched this operation will realize at once this procedure, which is essential to the discovery and removal of a deep tumor, is practically impossible unless both lobes of the cerebellum are exposed and plenty of free space for the dislocation of the cerebellar hemisphere toward the middle line is allowed for. In the case here recorded, which was operated upon by Dr. Cushing, unless this procedure had been feasible, it would have been practically impossible to get access to the deep tumor, which lay at least three inches below the surface of the dura.

6. A study of the records of cases operated upon and here cited has shown that in many cases laceration of the acoustic or facial nerve has occurred during the removal of the tumor, and more frequently still, laceration of deep-lying bloodvessels has been attended by

<sup>21</sup> Surgery, Gynecology, and Obstetrics, 1906. This was a case first seen by me, in which I recommended the operation.

hemorrhage, not only difficult to control at the time, but subsequently leading to a fatal termination. Such hemorrhage can only be avoided by great care in the extraction of the tumor, by tying such vessels as are seen to pass into its space prior to its removal, and by a free access to the cavity after the tumor has been removed, so as to allow for tying any vessels that are still actively bleeding. If hemorrhage is entirely arrested at the completion of the operation, and no oozing occurs into the cavity left by the removal of the tumor, it is perfectly safe to close up the wound completely without drainage. This was done in the operation by Dr. Cushing, here described, with a consequent primary union of all the sutures in the scalp, with, practically, recovery from the operation on the twelfth day.

There appears to be no reason why the occipital bone should not be entirely removed from a patient. An osteoplastic flap is extremely inconvenient and practically impossible to make in this region of the skull, especially if the posterior portion of the foramen magnum is to be removed. The thickness of the muscle and fascia at the back of the neck is such that it gives adequate support to the brain, and the absence of the occipital bone consequently leads to no discomfort. In the patient whose history is here recorded, and who is now practically well, there has not been any pressure upon the scalp, there is no pulsation to be felt through the scalp, there is no weakness in the muscles moving the head, the hair has grown as thickly as ever, and in itself acts as a protector, and the patient suffers no inconvenience from the loss of her occipital bone.

**THE PATHOLOGY OF TUMORS OF THE ACOUSTIC NERVE.** The study of the nature of the tumors found and removed has an important bearing upon the prognosis in operations for brain tumor. A recent study of the pathology of acoustic tumors by F. Henschen<sup>22</sup> has shown that of 145 such tumors examined, 133 were solitary and 12 were multiple.

As regards the solitary tumors, it is interesting to note that a large majority were fibromas or fibrosarcomas, or cysts, encapsulated, non-adherent, and, from the standpoint of the pathologist, removable surgically. It is, therefore, evident that the danger of relapse after an operation for an acoustic tumor is far less than in cases of tumors elsewhere. Henschen calls attention to the fact that the acoustic nerve is the only cranial nerve frequently affected by a tumor. He brings this fact into relation with the observation that in embryonal growth the bone tissue which surrounds the acoustic nerve is formed later than that about the other cranial nerves, at their exit, and hence that embryonal connective tissue persists around this nerve later than elsewhere. He shows that tumors of this nerve usually (in 8 cases out of 9 examined by him) have a small pedicle entering the acoustic foramen or internal

<sup>22</sup> Hygieia Festbund, 1909, No. 14.

auditory meatus, the nature of which is fibrous, and he suggests that it is the proliferation of this fibrous embryonal connective tissue which gives rise to the tumor. In 83 of the 145 cases examined by him such fibrous tissue was found in the tumor.

As regards multiple tumors of the acoustic nerve, these have been observed not only by Henschen, but by many others.

Henneberg and Koch<sup>23</sup> made a large collection of tumors involving the cranial nerves, especially the nerves in the cerebellar pontine angle, occurring as part of a general neurofibromatosis. They showed that tumors of this angle may be multiple, occurring in some cases on both sides, and Umber<sup>24</sup> records a similar case. Funkenstein<sup>25</sup> also records a case of bilateral tumors in the pontine angle which were found at an operation; both tumors were removed, and the patient died with respiratory paralysis soon after the operation. He reports at the same time four other cases, with autopsy, in which no operation was attempted. Sachs<sup>26</sup> has reported a case of multiple tumors in the pontine angle.

The possibility of such multiple tumors has always to be regarded in making a diagnosis, especially as symptoms referable to the cranial nerves on both sides have not infrequently been observed, but bilateral symptoms do not always indicate multiple tumors. In cases with autopsy it has been found that pressure of the tumor upon one side not only implicated the nerves upon that side, but also displaced the pons and medulla toward the opposite side so as to cause compression of the cranial nerves upon the side opposite to the tumor, thus producing the bilateral symptoms. This fact should not, therefore, preclude operation.

The frequency with which cysts occur in the cerebellar pontine angle is not to be overlooked.<sup>27</sup> And this fact leads me to mention the advisability of an exploratory puncture of the brain prior to a more extensive operation, as having a very direct importance in cases of tumor of the acoustic nerve. While it is well known that puncture of the brain through a very small hole in the skull by an aspirating needle, long ago suggested by Dr. Robert Abbe in this city, but recently performed and urged by Neisser and Pollack,<sup>28</sup> and by Pfeiffer,<sup>29</sup> is being constantly performed in German clinics, I have not found any records of its adoption in this country. Experience in Germany has shown that it is a harmless operation. The scalp is frozen, a small gimlet or drill is driven through the skull, a guard preventing its puncture of the dura, a small cannula with oblique end is pressed into the brain, and aspiration is employed

<sup>23</sup> Arch. f. Psych., 1902, xxxvi, 251.

<sup>24</sup> Neurolog. Zentralbl., 1907, p. 91.

<sup>25</sup> Mittl. aus der Grenzgeb. d. Med. u. Chir., xiv, 157.

<sup>26</sup> Jpur. Nerv. and Ment. Dis., 1906.

<sup>27</sup> See Scholz, quoted by Henschen, Hygeia Festbund, 1909, No. 14, where 75 cases are analyzed.

<sup>28</sup> Mittheilungen aus d. Grenzgeb. d. med. u. Chir., 1904, xiii.

<sup>29</sup> Arch. f. Psych., xlii, 2.

by a syringe. Thus, a small cylinder of brain tissue is obtained which may reveal tumor elements; or a cyst may be tapped which can readily be emptied by the aspiration.

Baisch<sup>30</sup> reports 2 cases of acoustic tumor in which puncture revealed the existence of a cyst. In the first case the subsequent operation showed it to be a part of a glioma, which was successfully removed, with the recovery of the patient. In the second case the evacuation of the cyst through aspiration was followed by such marked improvement that no operation was found necessary, and the patient was reported as recovered. In view of these facts, is it not incumbent upon us to urge this method of diagnosis in all brain tumors?

TUMORS OF THE CEREBELLUM FOUND AND SUCCESSFULLY REMOVED, WITH RECOVERY OF THE PATIENTS FROM THE OPERATION.

- 1904. Stewart and Holmes, *Brain*, xxvii, 560. 11 cases.
- 1904. F. R. Fry, *Jour. Nerv. and Ment. Dis.*, March. Tubercular.
- 1905. Borehardt, *Arch. f. klin. Chir.*, lxxvii, 892. Cholesteatoma.
- 1905. Ziehen, *Medizinische Klinik*, p. 34. Glioma.
- 1906. Putnam and Waterman, *Jour. Nerv. and Ment. Dis.*, May. Sarcoma, cyst.
- 1906. Horsley, *Brit. Med. Jour.*, August 23. 9 cases.
- 1907. Homburger and Brodnitz, *Mittl. aus der Grenzgeb. d. med. u. Chir.*, xix, 2. 2 cysts.
- 1907. Auerbach and Grossman, *ibid.*, xviii, 1. Glioma.
- 1907. Schultze and Schede, *ibid.*, xvii, 617. Glioma.
- 1907. Bruce, *Annals of Surgery*, xlv, 550. Cyst.
- 1907. Rubritius, *Beitr. z. klin. Chir.*, lxiii, 447. Cyst.
- 1907. Oppenheim and Borehardt, *Berl. klin. Wochenschr.*, xlv, 875. Fibroma, sarcoma.
- 1907. Ziehen, *Archiv f. Psychiatr.*, xlv, 768. Glioma.
- 1907. Borehardt, *Archiv f. klin. Chir.*, lxxxi, 181. 3 cases.
- 1907. Poppert, *Deut. med. Wochenschr.*, p. 613. Fibroma.
- 1907. Ballance, *Some Points on the Surgery of the Brain*. Tubercle.
- 1908. Weisenberg, *Jour. Amer. Med. Assoc.*, No. 16. Fibroma.
- 1908. Baisch and Narath, *Beitr. z. klin. Chir.*, lx, 482. 2 cysts.
- 1908. Bramann, *Berl. klin. Wochenschr.*, August 10. 9 cases (3 relapses).
- 1908. Tietze, *ibid.*, Cyst.
- 1908. Adler, *ibid.*, Cyst.
- 1908. Foerster, *Berl. klin. Wochenschr.*, April 6. Cyst.
- 1908. Willy Meyer, *Jour. Nerv. and Ment. Dis.*, September, p. 584. Fibrosarcoma.
- 1909. Jones, *Boston Med. and Surg. Jour.*, August 26.
- 1909. Kuttner, *Allgem. med. Central Zeitungen*, lxxiii, 198. Glioma.
- 1909. Ziehen, *Medizinische Klinik*, No. 1. Cyst.
- 1909. Krause, *Hirn Chirurgie*, Berlin, 1909. Cyst.
- 1909. Cushing, *Interstate Med. Jour.*, St. Louis, September. 11 cases.
- 1909. Grinker, *Jour. Nerv. and Ment. Dis.*, May. Fibroma.
- 1909. Leischnner, *Arch. f. klin. Chir.*, lxxxix, 542. Sarcoma.
- 1909. Borehardt, Oppenheim, *Centralbl. f. Chir.*, April. 2 cysts.
- 1909. Starr and Cushing, *Present article*. Endothelioma.

TUMORS OF THE CEREBELLUM OPERATED FOR AND REMOVED, WITH DEATH OF THE PATIENTS.

- 1904. Stewart and Holmes, *Brain*, xxvii, 525. 6 cases.
- 1906. Horsley, *Brit. Med. Jour.*, August 23. 1 case.
- 1906. Funkenstein, *Mittl. aus der Grenzgeb. der med. u. Chir.*, xiv, 157. Neuroma.
- 1906. Rubritius, *Beitr. z. klin. Chir.*, lxiii, 447. Neurofibroma.

<sup>30</sup> *Beit. zur klin. Chir.*, 1908, lx, 482.



1906. Bruns, Neurol. Centralbl., p. 971. 2 cases.  
 1906. Borchardt, Arch. f. klin. Chir., Band lxxxi. 3 cases.  
 1906. Poppert, Deut. med. Woch., p. 613. 3 cases.  
 1906. Auerbach, Deut. med. Woch., p. 614. Sarcoma.  
 1906. Ballance, Some Points on the Surgery of the Brain (Macmillan). 2 cases.  
 1908. Martens, Berl. klin. Wochensh., August 10., No. 32, Glioma.  
 1908. Bramann, *ibid.* 1 case.  
 1908. Tietze, *ibid.* Tubercle.  
 1908. Kredel, Centralbl. f. Chir., April, 2 cases.  
 1908. Siemmerling, Berl. klin. Woch., p. 701. Sarcoma, fibroma.  
 1908. Henschen and Dahleren, Hygiea, No. 44. Cyst.  
 1908. Becker, Deut. Arch. klin. Med., Band lxxxix.  
 1908. Ebsberg, Jour. Nerv. and Ment. Dis., September, p. 586. 1 case.  
 1908. Weisenberg, Jour. Amer. Med. Assoc., January. 1 case.  
 1908. Hunt, J. R., Jour. Nerv. and Ment. Dis., September. 4 cases.  
 1909. Flatau, Neurolog. Centralbl., p. 399. 1 case.  
 1909. Boettiger, Neurolog. Centralbl., p. 167. Cyst.  
 1909. Krause, Hirn Chirurgie, Berlin, 1909, p. 141. 3 cases.  
 1909. Cushing, Interstate Med. Jour., September, xvi, 607. 3 cases.  
 1909. Lemois and Durand, Ann. des mal de l'Oreille, March. Glioma.  
 1909. Biggs, Lancet, July 3. Fibroma.  
 1909. Grinker, Jour. Nerv. and Ment. Dis., May, p. 304. 1 case.  
 1909. Leischner, Arch. f. klin. Chir., lxxxix, 542. Cystoglioma, Neurofibroma.

TABLE OF PERSONAL CASES.

No.	Name.	Age.	Situation.	Operation.	Result.	Surgeon.	Autopsy.
1	M.	30	L. hemisphere base and left pons	Tumor not found	Recovery from operation; death 7 days later	McBurney	Glioma.
2	W.	10	Cerebellar pontine angle	Tumor found and removed	Recovery from operation; death 14 days later	McBurney	Cystoglioma.
3	B.	7	Cerebellum and pons	Tumor not found	Died three weeks later	McCosh	Sarcoma.
4	G.	39	Cerebellum and pons	Tumor not found	Death 7 days after	Brewer	No autopsy.
5	C.	6	Cerebellum and pons	Bone only exposed; hemorrhage	Unknown; child taken home	McCosh	
6	G. K.	8	Cerebellum	Cystoglioma found and partly removed	Death 6 days later	McCosh	Glioma and cysts within it.
7	A. T.	11	Cerebellum	Removal of part of occip. bone; excessive hemorrhage	Improved; discharged one month later	McCosh	
8	L. H.	13	Cerebellum	Decompression; tumor not found	Improved for two years	Cushing	
9	W. F.	17	Cerebellum	No tumor found, decompression only	Death	Hartley	Sarcoma of optic thal.
10	G. H.	18	Cerebellum	No tumor found; bilateral decompression and some cerebellar tissue removed	Well	McCosh	
11	F. A.	32	Cerebellar pontine angle	Removal	Recovery	Cushing	
12	A. D.	20	Cerebellum	None	Death suddenly day before operation	McCosh	Glioma with cyst in cerebellum. No autopsy.
13	K.	17	Cerebellar pontine angle	None	Sudden death prior to operation	McCosh	

I have appended to this article the record of 13 personal cases of tumors of the cerebellum, in 11 of which an operation was performed, and in 2 of which sudden death occurred just prior to an operation which had been determined upon. Three of these cases (I, II, and III) were included in Frazier's statistics. Case VIII is included in the statistics of Cushing. The other cases have not been published.

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## THE TREATMENT OF HEMORRHAGE OF THE SPLEEN.

BY JOHN G. SHELDON, M.D.,

OF KANSAS CITY, MISSOURI.

THE treatment of traumatic hemorrhage of the spleen by the methods ordinarily advised and practised is, as a rule, unsatisfactory.

**SPLENECTOMY.** Splenectomy, which of course stops the bleeding, is, to say the least, an undesirable operation. It is associated with considerable shock, deprives the patient of an organ that may be of considerable physiological importance, and it is not always easily or quickly accomplished. The mortality following splenectomy for hemorrhage is approximately 50 per cent. if the operation is done soon after the injury occurs. Berger<sup>1</sup> collected eighty cases of wounds of the spleen treated by splenectomy not later than nine hours following the injury; in thirty-five of these death occurred within twenty-four hours.

**SPLENORRHAPHY.** The suturing of splenic wounds, recommended by Lamarchia, Madelung, and others, is an unsafe procedure. Its field of application is limited, and it cannot be relied upon to control hemorrhage in any case.

**SENN'S METHOD.** Senn<sup>2</sup> recommends that in selected cases of splenic wounds the margins of the wound should be crushed and sutured. This method succeeded in stopping the hemorrhage in seven dogs in which incised marginal splenic wounds had been made. The application of Senn's method is limited, and on account of the thinness of the dog's spleen as compared with the human organ, it is probable that the experimental work magnifies the practical utility of Senn's procedure.

**JONNESCO'S METHOD.** Ligation of the splenic vessels to control splenic hemorrhage, recommended by Jonnesco, stops the bleeding, but is followed by necrosis of the spleen, and in dogs results in death. Pirone suggested that after the splenic vessels had been tied, the great omentum might be utilized to supply nourishment to the organ, and thereby prevent necrosis. This I have tried on three

<sup>1</sup> Arch. f. Chir., Band xxviii, Heft 3.

<sup>2</sup> Int. Cong. of Med., Madrid, November 21, 1903.

dogs. In two of the animals the omentum was placed around the wounded spleen after the splenic vessels had been ligated. One dog died twelve hours later and the other died in thirty-two hours. In each the spleen was necrotic and showed no evidence of blood being supplied by the great omentum. In the third dog the omentum was too small satisfactorily to encircle the spleen. The animal died forty-eight hours after the splenic pedicle was ligated. The spleen was necrotic throughout.

**OTHER METHODS.** Tamponing, the use of the cautery as recommended by Rehn, the use of hot air and steam recommended by Snegnireff, and the injection of heated air into the abdominal cavity advised by Kelling to control splenic bleeding, would seem too insecure for practical work. The work of Hartin Jordan,<sup>3</sup> who has successfully done partial resections of the spleen in dogs, indicates that resection may be utilized in treating certain splenic wounds.

The results obtained by the methods afore-mentioned show that in 168 splenic wounds collected by Berger, 86.3 per cent. died from hemorrhage within twenty-four hours. An attempt to make it possible to reduce this mortality in the future has been the stimulus that has led to the presentation of a method for treating splenic wounds that has not, to my knowledge, been described.

**METHOD ADVISED.** The procedure that I shall describe for the treatment of wounds of the spleen consists of the application to the splenic pedicle of a large flexible clamp, the blades of which are protected with rubber tubing, sufficiently tight to occlude the vessels but not to crush them. This clamp protrudes through the abdominal incision and is left in place for four hours. Then it is unlocked. If no bleeding occurs—as can be determined by the appearance of fresh blood in the wound, and the condition of the patient—the clamp is removed. The splenic wound is not treated in any way. After the splenic circulation has been shut off by the clamp, the vessels in the splenic wound empty themselves by draining into the peritoneal cavity and their cut ends are occluded by nature sufficiently firmly in four hours to prevent bleeding when the splenic circulation is reestablished by removing the clamp. If the wounded splenic vessels are prevented from emptying themselves, which can be done by tamponing or suturing the wound, the thrombosis started at the splenic wounds extends to the clamp on the pedicle and prevents the reestablishment of the splenic circulation after the clamp has been removed.

*Principles Involved.* The principles involved in the method herewith described are active in almost every surgical undertaking. The occurrence of the spontaneous arrest of hemorrhage is generally admitted. I think it can also be stated without argument that the

<sup>3</sup> *Lancet*, January 22, 1899.

escape of blood from the severed vessels is a most potent factor in preventing the spontaneous arrest of the bleeding by mechanical washing away the beginning thrombus. The arrest of the circulation through a severed vessel removes this obstacle to thrombosis and permits a rapid closure of the vascular wound. This is shown in wounds of the extremities in which hemorrhage has been controlled by elastic constriction above the wound. In such cases, if the constrictor has been placed a few hours, many times no bleeding occurs after its removal, even when vessels of considerable size have been severed. I have seen, in one case, spontaneous occlusion of the popliteal artery. A car wheel completely divided this vessel one inch above the knee joint. A constrictor applied to the thigh controlled the hemorrhage, and when the constrictor was removed six hours later, the divided artery and veins did not bleed. I have severed three femoral arteries in dogs and have applied protected clamps to the vessels about two inches above the wounds. Removal of the clamps four hours later was followed by no hemorrhage from the divided vessels.

In applying this principle to the spleen, experimentation was necessary to determine the length of time that the forceps should be left in place to permit a firm occlusion of the wounded splenic vessels. The spleens of two medium sized dogs were wounded by making two incisions on the outer surface of each spleen about two and a half inches long and nearly through the thickness of the organ. One wound was made in the longitudinal direction, the other very obliquely. The clamps were removed in six hours, and the bleeding was completely and permanently arrested. In two other dogs, very deep wounds were made at the middle of the spleen. There was no bleeding after the clamps were removed six hours later. In five dogs, incised splenic wounds were made (usually two large wounds in each organ) and the clamps left in place four hours. In no case did hemorrhage follow removal of the clamps. In one dog, three deep wounds were made in the spleen and the clamp removed at the end of three hours. Apparently no bleeding followed, but when the dog was killed one week later, a clot one inch in diameter was found in one of the wounds and the omentum was adherent around the clot. Clamping of the splenic pedicle for from three to six hours in ten dogs was followed by spontaneous permanent arrest of the bleeding in each instance.

*Reestablishment of the Splenic Circulation.* In the spleen of ten dogs, the splenic circulation was completely reestablished after the clamps were removed. This was shown by histological examination of the organs—the dogs being killed from twelve hours to three weeks after the experiment. The vessels at the site of clamping showed no evidences of injury. The intima was smooth in every case. In the dogs killed earlier than one week, the site of clamping could be located, but in those killed later it was impossible to

determine that a clamp had been applied. The splenic wounds in the dogs killed early were covered with plastic material; later complete healing by fibrous tissue was observed, and in two instances of gaping wounds the great omentum was adherent in the wounds. It seemed evident that the thrombosis in the splenic wounds did not extend beneath the surface, as the spleens were macroscopically and histologically normal close to the incisions. It would seem then that the splenic vessels distal to the clamp were emptied by being drained through the wound into the peritoneal cavity, and for this reason they did not thrombose or prevent a reestablishment of the circulation. If some of them did not drain and remained filled with stagnant blood, thrombosis would not be expected, as it was shown by Senn and Bumgarten that stagnant blood in a vessel, the intima of which was uninjured, did not clot. Now, if the splenic vessels are not allowed to drain, but are kept filled with blood, the thrombosis started at the wound extends in a proximal direction, and may even extend to the clamp—preventing the reestablishing of the splenic circulation, and resulting in partial or complete splenic necrosis. This was determined by suturing the splenic wound and then applying a clamp to the splenic pedicle. In four dogs, two incised wounds were made in the spleen. One was sutured; the other left open. A clamp was applied to the pedicle. In these specimens, necrosis was found in the portion of the spleen in which the sutured wound was located, while the tissue about the open wound was normal. In one dog, two splenic wounds were sutured and a clamp applied. The animal died on the fourth day from peritonitis. The spleen was necrotic, and the splenic vessels occluded by a thrombus. From the foregoing, I conclude that if a clamp is to be applied to the splenic pedicle to control hemorrhage, the splenic wounds should not be sutured or packed, but the cut vessels should be allowed to empty themselves—otherwise thrombosis and more or less splenic necrosis may be expected.

*Splenic Necrosis.* In none of the experiments performed was there evidence obtained that would suggest that anemic necrosis of the spleen might be expected to occur after the circulation had been shut off for six hours. If, however, the clamps are left in position for ten hours, necrosis may be expected. In two dogs the clamps were left in place ten hours. One died on the fourth day, the other on the sixth. In both the spleens were markedly necrosed, especially around the wounds. But as an anemia of four hours' duration seems sufficient to control splenic bleeding, and if splenic anemic necrosis does not follow unless the circulation has been shut off for more than six hours, the danger of splenic necrosis offers no barrier to the practical application of this method.

*Technique.* In making use of this method to treat splenic wounds, it is suggested that a flexible clamp be used, and the blades well

protected with rubber tubing. The pedicle should be clamped only sufficiently tightly to stop the bleeding, although considerable pressure is necessary to injure the intima sufficiently to result in thrombosis. The clamp should be left in place four hours, then loosened but not removed. If no bleeding occurs, the clamp may be removed; if the hemorrhage resumes, the clamp should be closed for another four hours. It would seem that this could be carried on for several hours, for the intermittent loosening of the clamp would renew the splenic circulation and prevent necrosis.

*Limitations of the Method.* It is not believed that this method is applicable in treating all splenic wounds. On account of the absence of, or slight, anastomosis between the splenic vessels, wounds severing large vascular trunks at or near the splenic hilum should be treated by splenectomy, for although clamping might stop the hemorrhage, splenic necrosis would follow. In all other wounds of the spleen, I see no objection to the application of the methods herewith described.

Since the foregoing was written no case of wound of the spleen has fallen into my hands, so I have not had an opportunity to test the method. Besides the experiments herewith recorded, eight additional similar experiments have been made; and, as the results and observations coincided with the previous work, they will not be described.

## REVIEWS.

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SEMMELWEIS. HIS LIFE AND HIS DOCTRINE; A CHAPTER IN THE HISTORY OF MEDICINE. By SIR WILLIAM J. SINCLAIR, M.A., M.D., Professor of Obstetrics and Gynecology in the University of Manchester. Pp. 369; 2 illustrations. Manchester: The University Press, 1909.

IN the rush and hurry and necessary overcrowding of the medical curriculum of the present day, it seems in vain to hope for any adequate consideration of the lives of the great in medicine; we wish, therefore, that it were possible to place this book in the hands of every doctor in America. It may be likened to a photograph of some wonderful monument. It is certainly a great tribute to the author that, after finishing the reading of the work, the reviewer found himself absolutely unable to criticise its technique, since he was left with but an imperfect idea of the constructive details of the book, having been entirely engrossed by the wonderful appeal of the story of Semmelweis. "In the history of midwifery there is a dark page, and it is headed Semmelweis," and the fact that a great deal of the personal suffering and misrepresentation could have been avoided by a man of a different mental make-up does not lighten the blackness of the story.

"Theology had a Luther, physical science a Galileo, biology a Servetus, but in the history of obstetrics there has been but one Semmelweis." The volume opens with an introductory section dealing with the early life of Semmelweis; this is followed by a chapter upon his life as an interne in the Vienna Maternity Hospital, an account of the doctrines prevalent before his time relative to the etiology of puerperal fever, some account of his early professional friends, and a most interesting description of the deductive reasoning employed in arriving at the conclusions which constitute the "Lehre." The remainder of the body of the work is taken up with a consideration of the attitude of the profession of the day with regard to the discovery, and quotations are given from the voluminous correspondence between Semmelweis and his most noted adversaries and adherents, the latter being sadly few in comparison. In considering the attitude assumed by the profession in America, the author devotes several pages to the well-known contribution of Holmes, stating that "if Semmelweis could have written

like Holmes, his *Ætiologie* would have conquered Europe in twelve months," but affirming with considerable heat that any comparison between the services rendered by Semmelweis and Holmes is preposterous. We assume from the prominence given by Sinclair to the matter that somewhere and somehow he must have gained good and sufficient reasons for the outburst, but we believe that all intelligent members of the profession are well informed as to the part played by the essay on the "Contagiousness of Puerperal Fever." There can be no question as to the great influence exerted by it at a time when the obstetrical seats of the mighty were occupied by crystallized obstructionists, and no one would have been less likely to have claimed scientific equality with Semmelweis than the genial "Autocrat." On the other hand, we have enjoyed the justifiable arraignment of other members of the American profession of that day, but we feel that the animadversions upon Holmes are unnecessary.

Doctor Sinclair deserves the thanks of the whole English speaking profession, and we feel sure that the perusal of the work will not be limited to them, for having brought the story of this life within their reach. It is a sad story, and it does not make very pleasant reading. It is not the story of Jenner, of Lister, or of Morton, all of whom saw at least in part the results of their labors: but it is the story of a man led by his love of humanity into attacking conditions which seem at the present day beyond imagination; it is the story of a man endowed with a mind which would not allow the supine acceptance of the dictum of authority, but who through his unaided observations obtained conviction in the face of persecution: and finally it is the story of a man dying insane after his whole life had been embittered by the neglect, not of himself—for no one can read this history without being convinced that he realized the greatness of his discovery and never for long doubted his ultimate triumph—but embittered by the neglect of his teachings with the consequent continuance of the slaughter which it had been his lifelong aim and hope to eradicate.

W. R. N.

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THE ELEMENTS OF HYGIENE FOR SCHOOLS. BY ISABEL MCISAAC.  
Late Superintendent of the Illinois Training School for Nurses.  
Pp. 172; 31 illustrations. New York: The MacMillan Co., 1909.

IN her book on *Hygiene*, Miss McIsaac has succeeded in presenting the subject, divested of much needless detail, in a way so concise and clear as to render it at once interesting and easily understood by the average pupil in our elementary schools. Before proceeding with the subject of hygiene proper, the author wisely devotes a



chapter to the subject of bacteria. She points out the vast economic value of bacteria as well as their pathogenic properties, and emphasizes the all-important role played by bacterial activity in the maintenance of life upon the earth. The chapter on food is comprehensive, being divided into five sections which deal with the relative value of various dietaries, the preparation of food, and the preservation and adulteration of food. Relatively too much space is devoted to the consideration of the latter subject. Though it is undeniably important, it seems unnecessary to quote at length, for the benefit of elementary students, from government reports, as to what is technically understood under the law by the terms "misbranded" and "adulteration." Climatology and ventilation, including heating and lighting, are next discussed; then follows a consideration of the subjects of water supply and filtration and the disposal of sewage and garbage. After taking up personal, household, and school hygiene from a useful, practical standpoint, Miss McIsaac discusses the effect of occupation on health, especially calling attention to the present status of child labor and the employment of women in the United States. A consideration of the various methods of disinfection and quarantine concludes the book. It is worthy of comment that in the entire book less than two pages are devoted to the alcohol question. Furthermore, the writer unhesitatingly quotes the dictum of Liebig, who held that "The use of spirits is not the cause but the effect of poverty." Here is, indeed, moderation, as rare as it is praiseworthy when encountered in a school text-book, the majority of which contain the most flagrant misrepresentations of the facts regarding alcohol.

On the whole, Miss McIsaac has well summarized the important phases of hygiene, and has, in addition, introduced much information on practical details which should make her book of value not only to the student, but also to teacher and parent. G. M. P.

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HYGIENE FOR NURSES. By ISABEL McISAAC. Pp. 208. New York: The Macmillan Company, 1908.

BACTERIOLOGY FOR NURSES. By ISABEL McISAAC, of New York. Pp. 179. New York: The Macmillan Company, 1909.

ANATOMY AND PHYSIOLOGY FOR NURSES. Compiled by DIANA CLIFFORD KIMBER. Third edition, revised by CAROLYN E. GRAY, R.N., Assistant Superintendent of the New York City Training School for Nurses. Pp. 438; 212 illustrations. New York: The Macmillan Company, 1909.

MISS McISAAC'S *Hygiene for Nurses* is an excellent little book, well adapted to its purpose—that of providing for the young pupil nurse a text-book practical and within the range of her daily work

and power of assimilation. It contains brief accounts of food, air, soil, water, sewage, garbage, the causes and dissemination of disease, personal hygiene, household hygiene, school hygiene, the hygiene of occupation, the employment of women and children, disinfection, and quarantine. The statements have been in large part drawn from the works of standard authorities, but all have been well arranged and tinged with the sane advice and practical experience of the authoress.

Miss McIsaac, well and favorably known as the author of *Primary Nursing Technique, Hygiene for Nurses, and Hygiene for the Use of Public Schools*, has prepared what should prove to be an exceedingly useful book on bacteriology for nurses. It discusses in plain and simple language the essentials of the structure, mode of development, and composition of bacteria, the effect of physical and chemical agents on bacteria, the effects of bacterial growth, the relation of bacteria to disease, immunity, inflammation, suppuration, the infectious diseases, and bacteria in the air, soil, water, and food. In addition, there is a schedule for twelve laboratory exercises of two-hour periods, which, however worthy the object sought to be subserved, seems somewhat in advance of the real needs of nurses. The book, nevertheless, is to be commended.

It suffices, perhaps, to mention the publication of a new edition of Miss Kimber's *Anatomy and Physiology for Nurses*, since the book itself is one of the best known and justly prized on the subjects of which it treats. Miss Gray, in preparing the new edition, has added the Basle nomenclature as far as practicable, a preliminary chapter on physical, chemical, and biological definitions, explanatory notes, summaries at the end of each chapter, and a number of new illustrations. We may say that a really good book has been made better.

A. K.

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PRACTICAL GYNECOLOGY. A MANUAL FOR NURSES AND STUDENTS. By NETTA STEWART, Sister in the Gynecological Wards of the Royal Infirmary, Edinburgh, and JAMES YOUNG, M.B., F.R.C.S.E., Clinical Tutor in Surgery and late Resident Gynecologist, Royal Infirmary, Edinburgh. Pp. 327. New York: William Wood & Co., 1909.

THERE is an unfortunate and no doubt unintentioned deception in the title. It is not a practical gynecology in any sense of the term. It had better have been given a title more definitely descriptive of the actual contents and scope of the book. A short chapter upon the anatomy of the pelvis is followed by a description of the more commonly used instruments. Asepsis, the method of the examination of the patient, a description of the vaginal douche,

of the method of catheterization of the bladder and of its examination, and the usual methods of local treatment follow. The remainder of the book contains a short study of gonorrhoea, of certain of the more common operative procedures, together with the preparation and after treatment of celiotomy cases, and finally a short glossary. We believe the book to be a good one to place in the hands of nurses, and there are many points without doubt of value to the student: but we reiterate, that the title *Practical Gynecology* is entirely too pretentious, and we do not understand under what form of medical instruction it could be needed by the student of medicine, as all it contains, except the points upon nursing, forms but a small part of the ordinary text-book.

W. R. N.

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HUMAN PHYSIOLOGY. AN ELEMENTARY TEXT-BOOK OF ANATOMY, PHYSIOLOGY, AND HYGIENE. BY JOHN W. RITCHIE, Professor of Biology in the College of William and Mary, Virginia. Illustrated by Mary H. Wellman. Pp. 362; 157 illustrations. Yonkers-on-Hudson, New York: World Book Company, 1909.

To all acquainted with the average "school physiology" and its inaccuracies, Prof. Ritchie's work must come as a welcome and long-needed advance. Not only has he given a concise account of the more important aspects of human anatomy and physiology, but he has succeeded in emphasizing many of the fundamental principles of biology, unfortunately too rarely brought to the attention of our school children. In addition, he has devoted a considerable portion of his text to a discussion of the elements of hygiene, and the acute infectious diseases.

In spite of the brevity which of necessity marks the anatomical and physiological descriptions, surprisingly few important phases of the subject are omitted. Occasional omissions, however, do occur. For example, in the description of the gastric juice, no mention is made of rennin; nor is the glycogenic function of the liver explained, the reader being left with the impression that glucose as such is stored in the liver. After disposing of the anatomy and physiology of a group of organs, the author discusses the hygienic measures necessary to maintain these organs in a state of efficacy and health. In this connection attention should be called to the chapter on ventilation following the consideration of the respiratory tract and an equally important one on dietetics that concludes the discussion of digestion.

The attention paid the comparative anatomy and biology is decidedly the most admirable feature of the book. The facts are stated in a way well calculated to awaken in the student an interest in all natural phenomena. Comparisons are drawn between the

skeletons, gastro-intestinal tracts, nervous systems and other organs of the several classes of vertebrates, thus making clear in a striking manner the various portions of the lower animals that have their homologues in man.

Much discredit has been brought upon elementary text-books of physiology because of the gross misstatements and inaccuracies with which they abound in reference to the effects of alcohol and tobacco. Although, in the present instance, the author has neglected no opportunity to emphasize the evils which may result from the use of these drugs, he has been content to adhere to known facts, without resorting to fanatical misrepresentation. At times his statements tend to be too sweeping, as when he says that practically everyone who uses alcohol uses too much of it, but upon the whole his views are in accord with the opinions held by recognized clinicians and pathologists. As a clear, accurate summary of the structure, functions, and hygiene of the human body, well adapted for schoolroom use, Prof. Ritchie's *Physiology* can be unhesitatingly recommended.

G. M. P.

THE OPEN-AIR TREATMENT OF PULMONARY TUBERCULOSIS. By F. W. BURTON-FANNING, M.D., F.R.C.P., Honorary Visiting Physician to the Kelling Open-air Sanatorium. Second edition; pp. 184; 6 illustrations. New York: Paul B. Hoeber, 1909.

THE book possesses merit, for it is a rather concise portrayal of the conditions incident to open-air treatment in pulmonary tuberculosis. A very thorough discussion of the subject of temperature is taken up, and especial emphasis is properly laid upon the value of the rectal temperature. The essential factors of open-air treatment, "air, rest, feeding, and supervision," are indeed requisites. The subject of home treatment is admirably considered, but it is accompanied by an unfortunate paucity of illustrations. Along certain lines the author asserts himself quite dogmatically. The theory of latent tuberculosis is unjustifiably upheld, and that of case-to-case infection is blotted out of consideration. It has been definitely shown that a 2 per cent. solution of chlorinated lime is inadequate to kill tubercle bacilli; yet this is recommended by him as a thorough disinfectant. His method of recording physical signs offers no advantage over the already existing schemes. Not a few statements are inconsistent, as, for example, advising spirits to be taken with milk and then deploring their use, etc. He is overenthusiastic upon the subject of opsonic work, this section having been added to the text of the first edition. The subject is attractively, concisely, and systematically presented, but a closer inspection reveals many inconsistencies.

W. T. C.

A MANUAL OF CHEMISTRY. By W. SIMON, Ph.D., M.D. Ninth edition; pp. 716; 78 illustrations and 8 colored plates. Philadelphia and New York: Lea & Febiger, 1909.

IN this edition Dr. Simon, assisted by Dr. Daniel Base, preserves the same high level of work which has characterized the previous issues of his *Manual of Chemistry*. The book is essentially a guide for beginners in chemistry, but is also adaptable for students of medicine, pharmacy, and dentistry. For the latter it will be found to be more valuable as a reference work than as a text-book, since more space is devoted to inorganic chemistry than is desirable in a manual to be used by medical and dental students. To this part of the subject nearly four hundred pages are devoted. The consideration of carbon compounds is very well done in the small space allowed, and what is there offered is well chosen. A short description of all the essential groups of organic chemistry is given and is quite clear enough for the beginner in the subject. The manual closes with a brief outline of physiological chemistry (100 pages), which perhaps is too brief, but may serve as an introduction to the subject. The book well merits the favor that has been bestowed upon it.

E. H. G.

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HANDBOOK OF DISEASES OF THE RECTUM. By LOUIS J. HIRSCHMAN, M.D., Fellow of the American Proctologic Society; Lecturer on Rectal Surgery and Clinical Professor of Proctology in the Detroit College of Medicine, etc. Pp. 374, with 145 illustrations and 2 plates. St. Louis: C. V. Moseby Medical Book and Publishing Co., 1909.

THIS work was written, we are assured by its author, to enable the family physician to treat the commoner rectal diseases with intelligence and success. Its aim is therefore commendable; but there must arise some question of the ability and advisability of the general practitioner converting himself into the character of an amateur specialist, if the expression be allowed. The poor, ignorant, general practitioner, on whose shoulders the burden already is so heavy, is here told not only the proper arrangement of offices, consulting room, toilet room, retiring room, etc., for "one who expects to do minor surgery or treatment work," but he is also specially instructed as to the size of the rooms to be employed: "The room should be large enough so as not to be uncomfortably crowded with the furniture and paraphernalia necessary, and yet small enough to be compact." This is a sample of the diffuseness manifest throughout the volume, which by such methods is expanded to a length of nearly 400 pages. While the author aims not to

describe any operative treatment which cannot be undertaken on patients treated as ambulatory cases, he includes in this category many procedures which are more safely performed only on those who may be kept in bed for some days subsequently, including a number in which usually a general anesthetic is to be preferred. The book is valuable in that it shows that much may be done to relieve and even to cure rectal diseases without radical operative treatment, and in that it demonstrates the efficiency of local anesthesia where usually a general anesthetic is employed. It is useless, so far as we can see, in that it neither will create rectal specialists worthy of the name, nor will be used by them; and it is harmful in that it tends to encourage incompetent charlatans to do work for which they have not been sufficiently educated previously, and for which the study of this volume alone is not a sufficient education. If rectal surgery is worthy of being considered a specialty, as is claimed by most of those competent to judge of the matter, then works such as this, which encourage amateur specialism, cannot be too severely condemned.

A. P. C. A.

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TUMORS OF THE KIDNEY. By EDGAR GARCEAU, M.D., Visiting Gynecologist to St. Elizabeth's Hospital and to the Boston Dispensary, Boston. Pp. 421; 72 illustrations. New York and London: D. Appleton & Co., 1909.

DR. GARCEAU'S book comprises a comprehensive discussion of renal, ureteral, perirenal, and adrenal tumors, as well as actinomycosis and echinococcus of the kidney. He has attempted to bring some order out of the chaos in which the classification of tumors of the kidneys is commonly involved, and in consequence he devotes considerable space to the hypernephromas, carcinomas, sarcomas, and malignant adenomas of the kidney. Although the distinction between the one or the other of these cannot always be made out, at least not readily, Dr. Garceau gives an excellent discussion of the etiology, pathology, symptomatology, physical examination, diagnosis, prognosis, and treatment; and he illustrates special points that he makes by the citation of cases. There are in addition chapters on embryonic tumors of the kidney, tumors of the renal pelvis and ureter, polycystic disease, and simple cysts of the kidney, and on tumors of the adrenal in adults and in children—all of which are really meritorious. The book ends with a chapter of some forty pages on the determinations of the renal efficiency. The author is much to be commended on the results of his efforts; the book is a worthy addition to contemporaneous medical literature.

A. K.

RATIONAL IMMUNIZATION IN THE TREATMENT OF PULMONARY TUBERCULOSIS. By E. C. HORT, B.A., B.Sc., M.R.C.P. Pp. 75; 29 charts and diagrams. London: John Bale, Sons, and Danielsson, Ltd., 1909.

FREQUENTLY repeated is the term "hetero-inoculation," which the author has coined to imply the inoculation of an alien product: it seemed advisable to employ this expression in order to overcome the rather confusing terminology. The chapter dealing with a personal investigation of the tuberculo-opsonic index reveals nothing of note, except a portrayal of the inconsistent results of different observers with identical serums. The author's idea in reference to the charting of evening temperatures only is very good, but the lack of consideration of the morning temperatures is inadvisable. Incorporated with the chapter on spontaneous and artificial auto-inoculation, there are 27 temperature charts of cases of pulmonary tuberculosis, enteric fever, scarlet fever, influenza, bronchopneumonia, and measles, the major part consisting of the first-mentioned. The interpretation of many of the phases is purely speculative. One patient received "graduated doses of auto-inoculation through auto-massage of his lungs." He rapidly improved. Favorable and fatal cases were studied and their charts compared. Isolated increments of temperature in otherwise declining phases were explained generally by auto-inoculation at such periods. This explanation is doubtless correct. It is questionable whether "hetero-inoculation" with tuberculin induces a rise of antitryptic activity in tuberculous subjects. It would seem that this depends largely upon the dosage. The chapter on autolysis is a very interesting resume. The book has brought forth nothing especially new along the prescribed lines. The confusion of certain terms is more apparent than real, for the previously mentioned coinage has served to elucidate matters. Otherwise, the subject has been very clearly stated and even though much of it is within the realms of speculation, it is one of the issues of today.

W. T. C.

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DISEASES OF THE NOSE, THROAT, AND EAR. By CHARLES HUNTOON KNIGHT, A.M., M.D., Professor of Laryngology in Cornell University Medical College, and W. SOHIER BRYANT, A.M., M.D., Senior Assistant Surgeon in the Aural Department of the New York Eye and Ear Infirmary. Second edition. Pp. 660; 239 illustrations. Philadelphia: P. Blakiston's Son & Co., 1909.

THIS is a second edition of Dr. Knight's volume on *Diseases of the Nose and Throat*, comprising 390 pages of the text, and an entirely new section on the ear, by Dr. Bryant, comprising the

remaining 219 pages of text. The usual general index is divided into separate indices for the nose, the pharynx, the larynx, and the ear, an arrangement in the reviewer's opinion more annoying to the reader than convenient.

As mentioned in the preface, Dr. Knight, in preparing this new edition, has made numerous minor changes throughout, the chief of which are to be found in the chapters on deviated septum of the nose and on diseases of the accessory sinuses. The illustrations of the entire chapters on the nose and throat are well selected, and some of them are original. We notice many familiar names, among them Schnitzler, Zuckerkandl, Hajek, Turner, Kriez, Bryan, and so on, and especially some of the admirable anatomical illustrations of Deaver, of Philadelphia. As the first edition of this work has already been reviewed in some detail in this JOURNAL, it merely remains to state that it has evidently been brought up to date of going to press, and thus maintains its excellent repute. Dr. Bryant's chapters on the ear present considerable originality. Each chapter is followed by a list of his own journal and other articles on the subjects discussed. He begins with the anatomy, development, comparative anatomy, and embryology of the ear. All this is beautifully, copiously, and instructively illustrated by numerous original drawings, and several ingenious series of diagrams. Indeed, we noted but two selected illustrations in the whole section on the ear; one, Oppenheimer's diagram of a mastoid operation when the bone involvement required exposure of the sigmoid sinus or the middle fossa of the skull; and the other, Whiting's illustration of a mastoid bandage applied so as to pass wholly above the sound ear. The first chapter is followed with chapters on physiology; theory of sound perception and allied topics; general pathology; the flora and fauna of the ear; etiology of ear affections; examination of patients and diagnosis, and succinct succeeding chapters on diseases, therapeutics, treatment, and surgical technique. The anatomical, biological, physical, physiological, and physio-pathological portions of the text are exceedingly interesting, and are treated largely in an original manner. They are sufficiently elaborate, some of them markedly so; but the text devoted to diseases proper is concise almost everywhere, and in most instances quite paragraphic, with the exception of the surgical technique in mastoid surgery, which is in sufficient detail to be very satisfactory, and is likewise admirably illustrated. Here attention is attracted to the author's modified mastoid operation, which leaves the ossicles in position when their condition justifies preservation. Under the caption special local therapeutics a number of formulas are presented for antiseptic, anesthetic, digestant, sterilizant, and other purposes. The final chapter describes numbers of special otological instruments, with illustrations of many of them, and a few diagrams of the manner and method of their usage.

J. S. C.



SHORT TALKS WITH YOUNG MOTHERS ON THE MANAGEMENT OF INFANTS AND YOUNG CHILDREN. By CHARLES GILMORE KERLEY, M.D., Professor of Diseases of Children in the New York Polyclinic Medical School and Hospital. Second edition; pp. 327; 21 illustrations. New York: G. P. Putnam's Sons, 1909.

THE ever-increasing appreciation on the part of the laity of the value of preventive medicine is in no way better shown than in the desire of intelligent mothers to learn how properly to care for their children. This modern demand for accurate knowledge has created a field of usefulness for such a book as Dr. Kerley's, the second edition of which has recently been published. In this compact volume the author explains briefly and clearly the best recognized scientific facts bearing upon the care and management of the child from its earliest infancy, both in health and disease. In so doing he dispels many of the traditional fallacies frequently adhered to by many a young mother. After describing the well baby and the necessary preparations that should be made for its reception into a household, he proceeds to devote nearly one-third of the book to a consideration of the all-important question of feeding. The section on "modified" or, as the author prefers to term it, "adapted," milk is an unusually clear, concise account of an ordinarily obscure subject. The author is to be further commended for having considered in detail diets suitable for children from one to six years of age. The frequency with which this phase of the feeding problem is neglected has resulted in widespread ignorance and indiscretions in the feeding of children after the first year. In addition to a careful consideration of the proper bathing, clothing, and exercising of the child, the remainder of the book comprises largely a series of brief descriptions of the more usual diseases of childhood. The attention paid to the serious complications of the acute infections conveys to the reader a true appreciation of their gravity; but the author wisely follows the rule of avoiding all suggestions relative to medical treatment. The freedom of the work from unexplained technical terms, the number of helpful practical suggestions it contains, and the fact that it is so evidently based upon the actual experience of the author, which has been considerable, should entitle the latest edition of this book to the deserved popularity enjoyed by its predecessor.

G. M. P.

# PROGRESS OF MEDICAL SCIENCE.

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## MEDICINE.

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UNDER THE CHARGE OF

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**The Association of Aortic Insufficiency with Syphilitic Aortitis.**—LONGCOPE (*Jour. Amer. Med. Assoc.*, 1910, liv, 118) reports twenty-one cases of aortic endocarditis associated with that type of mesaortitis, which is considered to be of syphilitic origin. All but three of these cases presented definite signs of aortic insufficiency during life. Seventeen of the patients were under fifty years of age, and in eleven a definite history of syphilis was obtained, or gummas were found at autopsy. A history of rheumatic fever was conspicuous by its absence. In seventy-six other cases of chronic aortic endocarditis, twenty-one, which showed lesions of other valves as well, and were for the most part almost certainly of rheumatic origin, had smooth, delicate aortas. In the other thirty-four cases, 66.6 per cent. of which were over fifty years of age, the chronic aortic endocarditis was in most instances associated with an arteriosclerotic process in the aorta, but not a true mesaortitis. In only four or 11.9 per cent. of these cases were signs of aortic insufficiency present during life. In all, of forty-three cases of true aortic insufficiency giving symptoms, eighteen or 41.8 per cent. were associated with mesaortitis, and of twenty-two cases of aortic insufficiency uncombined with lesions of any of the other valves, eighteen or 81.5 per cent. were associated with mesaortitis. From a therapeutic point of view the realization that so large a proportion of cases of pure aortic insufficiency are of syphilitic origin is of the utmost importance.

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**Dextrose Consumption by the Heart.**—Inasmuch as previous investigations as to the consumption of dextrose by the heart have given variable results, STEWART (*Jour. Exp. Med.*, 1909, xii, 59) has studied the

question in the isolated, perfused hearts of cats, and also of man. The perfusion apparatus used was that of Locke and Rosenheim—an arrangement by which a continuous circulation of fluid is kept up by means of oxygen pressure, so that the heart may be kept beating for many hours on a moderate amount of perfusion fluid. The quantity of dextrose in the fluid at the end of the experiment was compared with that at the beginning. The cat's hearts showed a consumption of dextrose proportional to the duration of the experiment and the weight of the heart. This amounted to 1.8 mg. of dextrose per gram weight per hour in freshly isolated hearts, and 1.3 mg. in hearts isolated two and a half hours after death. One human heart—that of a woman aged forty-six years,—was perfused at about two and a half hours after death. During the two hours over which the experiment was continued, 535 grams of dextrose were consumed, an amount equalling 0.07 mg. per gram weight per hour.

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**An Epidemic of Paratyphoid Fever Caused by a "Carrier."**—SACQUETEE and BELLOT (*Progrès médicale*, 1910, No. 3, 25) report an epidemic of paratyphoid fever occurring in a garrison of 250 soldiers. In the course of eight days, nineteen men became sick. The majority of the cases were typical, and ran a mild course, but a rather unusual feature was the prominence of meningeal symptoms—headache, Kernig's sign, stiff neck, and Babinski's sign. There were no fatal cases. Blood cultures were made in eight instances and in seven of these *Bacillus paratyphosus*  $\beta$  was isolated. The same organism was obtained from the stools in ten cases, and from the urine in two. The agglutination test was positive in dilutions varying from 1:350 to 1:900 with *Bacillus paratyphosus*  $\beta$ , but was negative even in dilutions of 1:50 and 1:30 with *Bacillus typhosus*, and *Bacillus paratyphosus*  $\alpha$ . Both food and water could be ruled out as possible sources of the infection, and it was then found that one of the cooks had suffered from a mild gastric upset, with headache, anorexia, and vague pains, several days before the epidemic began. In spite of his indisposition, however, he continued his work. Bacteriological examinations of his stools somewhat over two months after the onset of the epidemic showed the presence of *Bacillus paratyphosus*  $\beta$ . Similar results were obtained at intervals later. His blood serum agglutinated the *Bacillus paratyphosus*  $\beta$  in dilutions of 1:80, but failed to agglutinate typhoid or paratyphoid  $\alpha$  at 1:20. The authors consider that the cook had passed through a mild, unrecognized attack of paratyphoid fever, during which he had infected the men whose food he handled.

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**Purpura Hæmorrhagica Due to Benzol Poisoning.**—SELLING (*Johns Hopkins Hosp. Bull.*, 1910, xxi, 33) has studied a series of seven cases of purpura hæmorrhagica occurring in workers in a factory of tin cans, and apparently resulting from the use of a substitute for solder, which contained benzol. Two of the cases were severe, and proved rapidly fatal. The most remarkable feature was the blood picture, which was that of an aplastic anemia. The red cells showed only slight pallor and anisocytosis. Nucleated red cells were practically absent. The platelets were markedly diminished in number. There was a relative increase in mononuclear leukocytes, associated with an extreme leuko-

penia which reached, in one instance, 140 cells per c.mm. A series of similar cases was reported by Santesson, of Stockholm, in 1897. In these the etiological factor was benzol, which was used as a solvent for rubber. The injection of benzol, as well as of chemically pure benzene, into rabbits caused aplasia of the bone-marrow, and marked leukopenia, with only moderate action on the red cells. Other workers with benzol have reported the presence of hemorrhages following experimental injection.

**Intermittent Hydrarthrosis.**—Up to the present contribution, the literature contained reports of about seventy cases of recurrent effusion into joints, with little or no febrile disturbance, and no local signs of inflammation, the so-called intermittent hydrarthrosis. Examples of this disease fall into one of two main groups—the primary cases which come on without definite cause, and in which the joints recover completely in the intervals, and the symptomatic cases in which the joints have been more or less severely damaged by antecedent disease. While the majority of instances described hitherto fall into the former class, five of the eight reported by GARROD (*Quarterly Jour. Med.*, 1910, iii, 207) are of the symptomatic type. With Schlesinger, Garrod regards the condition as akin to the acute circumscribed œdema of Quinke, and cites other instances showing the relation of certain transient articular lesions to cutaneous lesions of the erythema group, that is, Henoch's purpura, erythema nodosum, the rashes of rheumatic fever. Moreover, circumscribed œdema sometimes exhibits periodicity, and certain angioneurotic disturbances met with in it have also been found in association with intermittent hydrarthrosis. In several cases already on record, the two conditions were associated in the same patient, and in one of Garrod's cases, effusion into knee and wrist joints was accompanied by recurring œdema of the eyelids. In two other cases there are charts showing remarkable regularity in the length of both attacks and intervals over periods of six and fourteen months respectively. In all cases met with by Garrod, either one or both knees were affected alone or in connection with other joints. Of concurrent conditions, pregnancy exercises the most influence on the course of intermittent hydrarthrosis. In almost every case in which pregnancy has intervened, the articular attacks have stopped during that period.

**Experiments on Secretory Gastric Stimulants.**—Pavlov, as is well known has shown that the secretory function of the gastric glands is dependent on two factors, a so-called "psychic" or "reflex" stimulus carried through the central nervous system, and excited by the sight, taste, or smell of food, and a so-called "chemical" stimulus due to the action of various chemical substances through the blood, substances found and existing pre-formed in the food, as in the case of various salts and extractives, or resulting from the decomposition of various albuminous bodies. BOLDIREV (*Russkyi Vrach*, 1910, etc.) has studied the relative stimulating effect on the gastric glands of decoctions of six kinds of fish, hare, beef, and chicken, and a solution of Liebig's extract, employing dogs with gastric fistula prepared according to Pavlov. Equal quantities of fish or meat broths respectively were introduced into the stomachs at a temperature of 38° C., care being taken to eliminate all psychic

factors. Comparing the action of fish broth, beef bouillon, and Liebig's extract, it was found that fish broth possessed the highest stimulating power on gastric secretion. Control experiments showed that the action was not due to salts or extractives in the broth, but to certain specific qualities of the fish broth. This activating power of fish broth varies for different kinds of fish—the broth made from the "chub" being the strongest, exceeding that induced by the same amount of beef bouillon both in quantity and in duration of its secretion. The pepsin content was slightly less per c.c., but increased absolutely in proportion, being as 96:99. The acidity in the case of fish broth was 4.5; in the case of beef bouillon, 3.8. A repetition of the experiment through many days failed to lessen the secretory activity of the stomach through a summation of stimuli as in the case of "psychic" stimulants; on the contrary, such repeated introductions of the broth heightened the irritability of the gastric mucosa, stimulating it even to more copious secretion. The author, therefore, suggests that in fish broths we may have an excellent stimulant to gastric secretion which does not lose its effect through its repeated use, and may, therefore, be of practical value.

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**The Action of Mercury on the Complex Hemolysis of Immune Serums and on the Wassermann Reaction.**—EPSTEIN and PRIBRAM (*Ztschr. f. exp. Path. u. Therap.*, 1909, vii, 549) find that small quantities of mercury accelerate and accentuate immune serum hemolysis in vitro, so that possible fixation of complement may be missed. They next attempted to reproduce the reaction in vivo. A rabbit was selected whose serum possessed the property, similar to that of luetic serum, of inhibiting hemolysis by the immune serum of a sheep, when treated previously with the alcoholic extract of a guinea-pig's heart. They found that the corrosive sublimate, which was injected subcutaneously, appeared in the blood of the rabbit in sufficient strength to inhibit complement fixation. The experiment seems to indicate that caution must be exercised in interpreting the disappearance of a previously positive Wassermann reaction in a patient under mercurial treatment. The disappearance of the reaction does not mean a cure necessarily; it may be due simply to the fact that enough mercury is circulating in the patient's blood to inhibit the reaction.

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**Studies on the Physiologically Active Substance of the Thyroid Gland.**—Since the experimental studies of the action of the thyroid gland and its products are based largely on surgical removal of the thyroid and the parathyroids as well, thus complicating the symptoms and making deductions unreliable, PICK and PINELES (*Ztschr. f. exp. Path. u. Therap.*, 1909, vii, 518) have re-investigated the subject. For their experiments they have used young goats, since it has been shown that in this animal the thyroid gland can be removed with comparative ease without injury to the parathyroids; furthermore, the clinical picture of myxœdema is well marked in the goat, especially when the gland is removed early in life. The thyroid glands used in the treatment of the thyroidectomized goats were obtained fresh from hogs. The authors have studied the therapeutic effect of the following substances: thyroid gland; iodothylin; thyreoglobulin; thyreoproteid; the products of peptic and tryptic digestion of the thyroid gland, including primary

and secondary albumoses and further cleavage products, obtained separately. They find that thyroid gland and thyreoglobulin have a marked and rapidly beneficial action. Secondary albumoses derived from hydrolysis of the thyroid are also active, but apparently less so than the former substances. Thyreoproteid, iodothyryn, and the less complex products of digestion of the thyroid were wholly inert. Their experiments offer no ground for the supposition that iodothyryn is the active constituent of the gland, or even that it is one of the active constituents. The authors believe, apparently, that iodothyryn is capable of stimulating the thyroid gland to increased activity and are inclined to attribute the favorable results in myxœdema reported in literature to stimulation of the gland itself, a part of which they assume has persisted, but is functionally insufficient.

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**Disinfection of the Skin with Tincture of Iodine.**—UNGER (*Berlin. klin. Woch.*, 1910, xlvii, 63) has tested the method of skin disinfection proposed by Grossich with good results. The field of operation is painted with tincture of iodine (10 per cent. to 12 per cent.), and after a few minutes (drying) it is repainted till the skin has the dark color of a negro. After operation the line of stitches is again painted. Better results are obtained when previous washing of the skin is omitted, the author says, the skin being shaved dry, when necessary. Numerous laparotomies have been performed after employing this technique with uniformly good results. The method should be valuable to the general practitioner in minor operations, such as pleural aspirations, infusions, etc., because of its simplicity and rapidity.

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**Bile Acids as a Cathartic.**—GLAESSNER and SINGER (*Wien. klin. Woch.*, 1910, xxiii, 5) have discovered that bile administered per rectum leads to prompt evacuation of the bowels. The action has been studied in detail in dogs, and it has been found that the peristalsis is set up chiefly in the large intestine. Bile acids are the active constituent of the bile. Cholic acid acts most powerfully, though taurocholic and glycocholic acids also cause active peristaltic movements. Because of its expense, the extensive use of cholic acid is precluded. "Platner's" bile has been found to be a suitable substitute, given in doses of 0.2 to 0.5 gram. As a rule, the patient has a stool in five to fifteen minutes after administration per rectum. The stool is formed, with no excess of fluid. The results have been especially gratifying in paralytic ileus, in post-operative and peritonitic intestinal paresis, and in atonic conditions of the large bowel.

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**The Lungs and Trauma.**—KÜLBS (*Archiv f. exp. Path. u. Pharmakol.*, 1909, lxii, 39) reports the pulmonary effects of trauma of the chest in dogs. In addition to pleural wounds, rather extensive lesions of the lung occurred. The usual finding was hemorrhage. The skin was often intact. At times the hemorrhage involved an entire lobe. Infection of the hemorrhagic area was not observed. That similar lesions occur in man as a consequence of blows with blunt instruments is quite possible, though conclusions cannot be drawn safely in this instance from the results of animal experiments. However, pneumonia following trauma occurs occasionally in man. It is probable that the immediate effect of

trauma in man and the dog is identical. In man, the liability to infection of the hemorrhagic zone is much greater. The pneumonia develops gradually, usually several days subsequent to the traumatism, probably from progressive extension of the bacterial infection.

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## SURGERY.

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UNDER THE CHARGE OF

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**The Etiology of Appendicitis.**—MACLEAN (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1909, xxi, 36) investigated the causes of appendicitis among soldiers and sailors, and restricted the investigation to the importance of a simple, infectious intestinal catarrh, intestinal worms, influenza, the mode of life, and the nourishment taken. A large number of cases of intestinal catarrh and dysentery were observed by MacLean in China, and he concludes that appendicitis occurs very rarely in these conditions. Nor does there seem to exist any special causal relation between typhus and appendicitis, or between the presence of intestinal worms and appendicitis. Likewise as between influenza and appendicitis, a causal relation can be excluded. The Chinese enjoy a rare immunity from appendicitis, which is regarded as the offspring of European culture. It has its essential cause in the different modes of life of cultured and uncultured people. When this difference in living between the people of nations free of appendicitis and those among whom it is common and increasing is investigated, it is found that it must lie in the difference in nourishment. It lies probably in the difference in the consumption of meat, which is greater among Western people than those of the East, greater among city people than country people, and greater today than one hundred years ago. It is generally known that appendicitis is a disease of the well-to-do, who eat more meat than the poorer people. Constipation is almost a national condition in Germany, England, and America. In China, except in opium smokers constipation is rare, which is also true of country people in general. The constipation associated with a meat diet disappears as soon as the physician enforces a vigorous vegetable diet. Mucous colitis is very frequent in the meat eating countries, but is very rare in the Chinese, colored people, and those who live in the country. MacLean has never seen it among the Chinese. It is well known that constipation, mucous colitis, and appendicitis are frequently associated. They should be

looked upon as the results of a predominating meat diet. This theory of chronic irritation of the lower bowel and its relation to appendicitis, explains some questions, previously unexplained. The infrequency of appendicitis in infants and young children is due chiefly to the fact that they are not meat eaters. Whatever preponderance of appendicitis occurs among military men is due to the fact that in the service, they eat more meat than at home. Men have the disease more frequently than women for the same reason, and the occurrence of the disease in several members of the same family, is to be explained by the fact that they all partake of the same excess of meat. In MacLean's opinion, therefore, an excessive meat diet is the underlying cause of appendicitis.

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**The Causation of Perforating Ulcer of the Foot.**—LEVY (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1909, xxi, 85) is inclined to view every genuine perforating ulcer as the result of a central nervous disturbance, since it is exceedingly difficult, probably impossible, in a multiple neuritis to exclude a central disease. Probably many cases reported in past years, of "perforating ulcer in neuritis," were in reality due to an unrecognized tabes. In the 12 patients presenting 14 perforating ulcers of the foot, typical arthropathies were present. The joints and bones participated in the process, with the exception of one case in which there was a spontaneous fracture. In one case of chronic ulceration of the toe in syringomyelia, no bone changes were manifest. The ulcer showed no signs, microscopically, of tuberculosis. In general, every chronic ulceration with simultaneous disease of the nervous system, should not be considered, a priori, as a perforating ulcer. The changes in the bones and the joint in Levy's cases were regarded as the primary condition, the perforating ulcer as a secondary result. Mechanical insults play only a predisposing role, and not a purely causal one. An exact clinical and x-ray examination should be made in all cases of perforating ulcer, and should determine the existence of these changes (arthropathies, synovial effusion, spontaneous fracture). When surgery is called upon as a therapeutic measure, the primarily diseased portions of the bones, which are the underlying cause of the perforating ulcer, should be removed.

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**Acute Primary Typhlitis.**—RÖPKE (*Archiv f. klin. Chir.*, 1909, xcix, 160) says that in the whole literature of acute inflammations of the right iliac fossa, cases of acute primary typhlitis are met with only very rarely. Many internists have denied the occurrence of this condition, while others admit that it does occur occasionally. Röpke reports four cases which were operated on for appendicitis and the diagnosis thus made. In one case in which there had been previous similar attacks, there was found to be a total obliteration of the appendix, which was probably due to the previous occurrences of appendicitis. The similarity of all attacks and particularly the occurrence with every attack of a troublesome diarrhoea, gives reason for the opinion that each attack of appendicitis had set up a severe inflammation of the caecum, especially as the appendix was free of adhesions. The inflammatory process in the right iliac fossa takes its origin in the great majority of cases from the appendix, but in rare cases it may come alone from the caecum. A stercoral typhlitis cannot be demonstrated with certainty. The typhlitis may be caused



by infection from the intestinal contents or by way of the blood or lymph paths. A sharp distinction cannot be made between typhlitis and appendicitis, the clinical symptoms of both being the same throughout. The treatment of acute typhlitis is essentially the same as for appendicitis. The appendix should be removed at every operation, even if it appears to be normal.

**Radical Operation for Non-incarcerated Hernia.**—IMFELD (*Deut. Ztschr. f. Chir.*, 1909, ciii, 57) makes a report on 454 hernias operated on in Kocher's clinic in Bern. There were 342 indirect and 24 direct inguinal, 38 femoral, 25 umbilical, 21 epigastric, and 4 ventral. The indirect inguinal hernia were operated on by four different methods. In most of the cases the invagination-displacement method of Kocher was employed. Here and there the lateral displacement method of Kocher, without invagination was performed. For those cases not suited to either of these methods, the so-called "old method" was done, and it was also used in children. It consisted in isolating and ligating the sac and then placing it in a high position, the canal then being sutured. Here and there the Bassini method was employed, but only in very rare cases was it the pure Bassini method. In the umbilical, epigastric and ventral hernias, the sac was removed and the ring closed. Two patients died, a mortality of 0.44 per cent. In most cases a hematoma developed, which was left alone, punctured and aspirated, or cleaned out. In 4 cases there was suppuration and healing by granulation, in all others by first intention. The best end results in the indirect inguinal hernias, were obtained by the invagination—displacement method, *i.e.*, 25.2 per cent. of permanent cures. In the femoral this method showed 94.45 per cent. of permanent cures. It was employed in only 3 direct inguinal hernias, and of these, 2 recurred, 33.3 per cent. of cures. With this method Hirschkopf operated on 83 cases and obtained 98.8 per cent. of permanent cures; Daiches, in 90 cases, obtained 96.7 per cent.; and Imfeld, in 247 cases in this series, obtained only 94.4 per cent. These poorer results are explained as follows: Two of the recurrences were in direct inguinal hernias, which are especially unsuited to this method; many of the operations were performed by assistants; the hernias in which there was no hernial sac were excluded from the series and these give the best results; and finally, Hirschkopf's reports concerned the cases, one to two years after operation, Daiches' five years after, and Imfeld's five to eight years after operation.

**The Treatment of Fracture-dislocations of the Spine with Compression.**—ROBERTSON (*Deut. Ztschr. f. Chir.*, 1909, ciii, 179) says that in every fracture of the body of a vertebra with compression of the cord by the bone, in which the diagnosis is established by the x-rays, a careful operation is necessary. The operation should aim to expose freely the site of the compression. A laminectomy alone is not sufficient, but the bone on the posterior surface of the wounded body must be excised to obtain positive results. The pairs of nerves immediately above or below the dislocated vertebra should be divided in order to prevent as far as possible angulation of the spinal cord and the dura. A preliminary hemostasis should be obtained, not only to make the operation more easy, but also to prevent the accumulation of blood, which may interfere

with the blood supply of this region. Provisional sutures are introduced on either side of the proposed incision, which on being tied will control the bleeding in the soft tissues. Adrenalin injections are employed to control the bleeding from the dura in the bone. The loss of cerebrospinal fluid in the days following the operation is not important, and any disturbance which may result from its loss can be overcome by hypodermoclysis. An effort should be made to provide immobility by a plaster cast, after operation, and even on the operation table.

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**The Treatment of Convulsions Following Orthopedic Operations.**—SCHANZ (*Zentralbl. f. Chir.*, 1910, xxxvii, 43) says that occasionally, shortly after an orthopedic operation, epileptiform convulsions occur, and sometimes prove fatal. They may occur on the same day or several days after the operation. Before the convulsion the patient may be apathetic, complain of severe headache, or be very cheerful. Frequently there is a sharp rise of temperature, at the beginning of the convulsion, which does not depend upon an infection. The convulsion is so similar to the epileptic type that they are frequently confused, and the relation between the convulsion and the operation is not suspected until a series of convulsions have taken place. The course of the cases vary. Of about 10 cases seen by Schanz, 1 died, 1 developed hemiplegia, and all the others recovered. Von Aberle has shown that the convulsions are due to fat emboli. Before he knew the cause of the convulsions, Schanz had employed subcutaneous saline infusions in the treatment and he regards the effects as evidently favorable; more favorable the earlier and the more abundantly they are given. He believes that the effect of the saline solution is to dilate and flush the capillaries in which the fat droplets are lodged, tending to thin out the fat emulsion and to force it onward. The rule in his clinic is to give immediately one-half to 1 liter of the saline solution, in different places. In a very severe case threatening the life of the patient, he would give the infusion intravenously.

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**A Contribution to the Operative Treatment of Epilepsy.**—E. BIRCHER (*Zentralbl. f. Chir.*, 1910, xxxvii, 5) after referring to the report of Krause on the results of excision of the brain centres controlling the convulsions, calls attention to the method of treatment employed by H. Bircher. This method is more simple and Bircher believes as effective as the Krause excision. The part of the brain involved is exposed freely by an osteoplastic flap. The dura will be found under strong tension, especially, in cases of genuine epilepsy, as Koehler and more recently Friederich and Krause have shown. The dura is then carefully opened, preferably, with a crucial incision, and the brain exposed. Now follows the important procedure of massaging the exposed brain surface. This is best done with the thumb, for three to five minutes, covers all the cortex in the opening, and has no regard for the pia mater. The dura is then closed or a drainage opening is left. It is absolutely necessary to open the dura, otherwise the desired result will not be obtained, as was shown after two operations on one case, in which after the third operation and the opening of the dura the attacks slowly disappeared and have been absent for four and one-half years. In three other cases the cure has lasted two and one-half, two, and one-half

a year. The effect of this treatment on the brain was shown in a case which came to autopsy eight weeks after operation. For four years the attacks had been increasing in frequency and severity and the patient would remain unconscious for several days at a time. Because of the marked brain pressure at the time of operation, the bone covering the opening was removed. Primary healing occurred. For two months there was no convulsion and then more severe attack than usual occurred. The patient died four days later in status epilepticus. The autopsy showed excessive tension of the dura and the ventricles were slightly enlarged. At the site of operation the healing was faultless with no dural adhesions. The whole circumference of the massaged surface of the brain could be mapped out. Its color was whitish, in contrast to the gray cortex, and the surface was sunken below that of the surrounding parts. A vertical section of the brain was made and it was seen that the massaged surface was reduced in thickness to about one-fourth of the normal. In the centre of this area the cortex had completely disappeared. Bircher thought that in this case death was due rather to an associated valvular disease of the heart than to the epilepsy. He believes that the massage brings about a gradual atrophy of the gray matter of the cortex and that it therefore produces the same result as excision of the cortex, without the motor and sensory paralysis which immediately follow excision.

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**Ureteral Calculi.**—JEANBRAU (*Ann. de. m. d. org. gén.-urin.*, 1910, i, 1 and 132), in an extensive paper on this subject, takes up the history, pathological anatomy, clinical aspect, diagnosis, skiagraphy, and therapy. He sums up the clinical picture according to the site of the calculus. (1) The functional symptoms in lumbar and iliac calculi and those of the upper part of the pelvic ureter are as follows: predominance of symptoms of a renal character; nephritic colic without results but with pain radiating down the ureter, or vice versa; spontaneous pain along a certain extent of the ureter after the crisis, persisting indefinitely with exacerbations due to movement, indigestion, etc.; microscopic hematuria after the crisis; and rarely vesical symptoms. (2) Functional symptoms of juxtavesical ureteral calculi; nephritic colic without results, and ureteral crises; pelvic pain, continuous or intermittent; vesical, seminal, testicular and rectal symptoms (Young). (3) Functional symptoms of ureteral and intravesical calculi: vesical symptoms, simulating a calculus of the bladder with pain at the end of the penis, burning upon micturition, dysuria, sudden arrest of the stream, polyuria on movement; seminal and testicular symptoms; nephritic colic without results and ureteral crises when the calculus obstructs the meatus; these symptoms are especially marked when there is an intravesical prolapse of the ureteral mucosa. When the calculus becomes blocked and immovable in the ureter, it increases progressively by crystalization upon its surface of urates, oxalates, or phosphates, and leads more or less rapidly to destruction of the kidney by pyonephrosis, by urenephrosis, vesical sclerosis and atrophy, periureteritis with ulceration, perforation of the ureter, perinephritic phlegmon and ureteral fistula, through which the calculus may be eliminated. Every calculus arrested in the kidney, proceeds to the complete destruction of the kidney which forms it. At the same time it prepares the anuria for the time when the ureter

will become obliterated. The ureter may be explored by palpation to find the painful area; and the calculus may be felt through the abdominal wall, by the vagina or rectum. The appearance of the ureteral meatus may lead one to suspect the existence of calculus higher up in the ureter, as has been shown by Fenwick and corroborated by Klotz. Exploration of the ureter by the ureteral catheter with a wax tip, will often show scratch marks on the wax when a stone is present. At times the catheter will pass the stone without receiving such marks. The  $x$ -rays have reduced considerably the indications for this method of diagnosis. In 64 out of 68 cases, the  $x$ -rays gave a shadow of the calculus. All calculi too large to pass spontaneously will give a skiagraph shadow, with some exceptions that remain to be studied. The causes of non-visibility of the stone are: (1) Faulty technique; (2) the chemical constitution of the stone; and (3) its small size. The chemical constitution plays the most important role. The stone may be removed by the superior orifice of the ureter after a nephrotomy or pyelotomy, by the inferior orifice after a cystotomy, or by incision of the ureter, uretero-lithotomy. Nephrotomy is indicated only when there is a period of anuria and when there coexists a stone in the kidney. Pyelotomy permits easy extraction if the pelvis is accessible and it is dilated. Extraperitoneal uretero-lithotomy is the operation of choice. When the patients are not anuric and have sufficient resistance not to succumb to the anæsthetic, uretero-lithotomy gives a mortality of 1.16 per cent. In 10 cases operated on in a period of anuria it gave 6 deaths, or a mortality of 60 per cent. Fistula formation will be avoided if the permeability of the ureter in its whole extent can be established after the removal of the calculus.

## THERAPEUTICS.

UNDER THE CHARGE OF

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**The General Principles of Vaccine Therapy.**—RICHARDSON (*Jour. Amer. Med. Assoc.*, 1910, liv, 255) points out the fact that in vaccine therapy the aim is the production of an active immunity. Therefore, success in this method of treatment presupposes that the patient is not already completely overwhelmed by the infection. Furthermore, if this procedure is to bring about, as it should, increased bacterial destruction, with the setting free thereby of an increased amount of endotoxin, this destruction must not be too rapid or excessive lest efforts to cure do harm through hyperintoxication. Bacterial immunity is brought about through the action of a great variety of different though related immune substances, and as a result of inoculation with vaccines there may be formed antitoxins, anti-endotoxins, lysins, agglutinins,

precipitins, opsonins, and other allied products. By bacterial vaccine is generally meant a culture of the special organism sterilized by heat, or otherwise, and suspended in known proportions in normal salt solution. Living organisms, attenuated either in number or virulence, have also been used. In this connection Richardson mentions the work of Strong, who inoculated plague bacilli of attenuated virulence in order to produce a stronger immunity. Living typhoid bacilli and tubercle bacilli have also been used and favorable results have been reported. Richardson says that autogenous vaccines are preferable to stock cultures. No definite rules can be laid down as to dosage. It is advisable to begin well below what is considered the ordinary dose and gradually to increase. The interval between doses will vary in different infections. The author calls attention to the inoculation against typhoid fever of large numbers of troops in the British Army, as reported by Leishman. Of 5473 soldiers inoculated, only 21 were subsequently infected, with 2 deaths, while of 6610 non-inoculated in the same regiment, 187 had typhoid and 26 died. The experience of the Germans, while not so extensive, confirms these results. Chantemesse and his colleagues used a serum treatment of typhoid fever in 1000 cases, with a death rate of 4.3 per cent. Of 5621 patients who were given routine treatment during the same time, 17 per cent. died. The nature of Chantemesse's serum is not understood, though he claims antitoxic properties for it. Richardson says that there can be little doubt that infections of the urinary tract due to the colon bacillus are favorably affected by vaccine treatment. Vaccines have also been used with favorable results in the treatment of gall-bladder fistula and in cases of appendicitis where pure cultures of colon bacilli were obtained.

**Subcutaneous Purgatives; a Clinical Study on Phenoltetrachlorophthalein.**—ROWNTREE (*Johns Hopkins Hospital Bull.*, 1909, ccxxii, 293) reports his results with the subcutaneous administration of phenoltetrachlorophthalein. He gave 0.4 gram dissolved in 20 c.c of oil hypodermically to patients suffering from chronic constipation. Ten out of twenty-five patients, after receiving one injection of this oil preparation, together with instructions as to diet, hygiene, and habit, have had no return of constipation. Rowntree gives the following disadvantages of the general adoption of phenoltetrachlorophthalein as a subcutaneous purgative: (1) The insolubility of the drug in water. (2) The slight degree of its solubility in oil, necessitating a large volume for injection. (3) The long time that elapses before the onset of purgation (eighteen to twenty-four hours). (4) The mild character of its action, which is laxative rather than purgative. The redeeming features are: (1) The prolonged nature of its action. (2) The absence of crampy pain and colic throughout the period of its action. (3) Its non-irritant action locally. (4) The constancy, at least in the cases so far studied, with which it has produced its result. (5) The non-toxicity of the drug. Rowntree says that it may prove of value: (1) In coma; (2) in marked gastrointestinal irritability when nothing can be given by mouth; (3) among the insane, who often refuse to swallow medicine and who fight against enemas; (4) in chronic constipation, together with hygienic, dietetic, and psychical treatment. Rowntree believes that it is worthy of a trial in the field of abdominal surgery, where its introduction under the skin

can be accomplished during the anesthesia without any pain whatever, and where its mild, prolonged, laxative effect, continuing for from four to six days, may possibly entirely dispense with the necessity of administering any purgative by the mouth during the first week subsequent to the operation.

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**Magnesium Poisoning.**—Boas (*Bost. Med. and Surg. Jour.*, 1909, cxi, 122) believes that magnesium poisoning is probably more frequent than is generally supposed, the true cause of the toxic condition remaining unknown in most cases. Boas reports three cases, two of which were suspected merely because of the high specific gravity of the urine. The specific gravity in one of these cases was 1070; in the other it was 1080. These two cases recovered, but the third case died. Fraser reports a case of his own and discusses six other reported cases. Boas has made a careful study of the ten available cases, and in addition carried out experimental work in order to determine the conditions governing the absorption of Epsom salt solutions. He found that in the absence of hydremia the tendency of magnesium sulphate to be absorbed increases with the concentration of the solution, the dry salt being completely absorbed without action on the bowels. This fact was shown by Hay to be true also of Glauber's salt. In hydremic conditions, however, the salt, even when it is given in very concentrated solution, is not absorbed. It appears, therefore, that the practice of giving very concentrated solutions of magnesium sulphate to deplete the system of excessive water is rational, but perhaps not without possible danger. In the absence of œdema or ascites, the object of giving magnesium sulphate can be none other than to produce efficient catharsis. To attain this object without the danger of intoxication from absorption, the salt is best given in solutions not exceeding 6 per cent. in concentration. Above this concentration more or less magnesium sulphate is absorbed, and its presence in the circulation is a menace to the patient's life. As a result of Boas' investigations, the ward patients in the Massachusetts General Hospital are now given one-half ounce of Epsom salt dissolved in three ounces of water, to be followed immediately by a glass of water.

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**The Action of Strophanthin.**—CRISPOLTI (*Il Policlin.*, 1909, xvi, 248) has made numerous experiments with Merck's and also with Böhringer's strophanthin. He gives as dosage by the mouth 1 to 4 mg., and up to 4 mg. a day; by intramuscular injection, 1 mg. and up to 3 mg. a day; by intravenous injection, 0.25 to 1 mg., and up to 2 mg. a day. Strophanthin is very uncertain in its action when given by the mouth, according to Crispolti; small doses are without any effect, while larger doses rapidly produce symptoms of intolerance. These symptoms are headache, a sense of tightness in the chest and over the precordium, marked slowing of the pulse, at times a bigeminal pulse, marked rise in the blood pressure, cardiac arrhythmia, insomnia, nausea, or vomiting. Such symptoms are less marked and more transient when strophanthin is given intravenously. Crispolti says that strophanthin is indicated in cases of heart failure with arrhythmia and low blood pressure, or in infective processes or myocarditis when the heart is giving out, and when an immediate effect is required. Given intravenously, strophanthin

should make the pulse slower, fuller, more regular; dyspnoea and cardiac oppression should be relieved, diuresis should set in, and the general conditions of the patient should improve markedly within a few hours. The dose should be 0.5 or 1 mg. in cases of severe heart failure; one injection a day is usually enough, but two may be given of 1 mg. each in bad cases. Four or five intravenous injections are usually sufficient. Intramuscular injections of from 0.5 to 1 mg. of strophanthin are indicated in the less severe cases of failure of compensation. Crispolti gives, as contra-indications to the use of strophanthin, high blood pressure and marked arteriosclerosis and acute or chronic nephritis.

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**The Intravenous Use of Strophanthin in Broken Cardiac Compensation.**—STONE (*Bost. Med. and Surg. Jour.*, 1909, xvii, 586) says that in certain cases the intravenous use of strophanthin has a most favorable effect in restoring cardiac compensation. The immediate result is to increase the amplitude of the pulse wave. The frequency of the heart is at the same time slowed within a few minutes, almost, if not quite, as completely as can be accomplished by the administration of digitalis preparations by the mouth in the course of several days. This immediate relief will last from twelve to seventy-two hours, and in some cases even longer, and is usually accompanied by free diuresis, or will permit diuretics previously inert to become once more active. Stone points out the dangers in the intravenous use of strophanthin, and says they must not be underestimated. The therapeutic dose and the poisonous dose are near together, and as the elimination of the drug is slow, one can easily get toxic symptoms of slowed pulse and of heart block from too frequent administration. The previous administration of digitalis is an almost sure contra-indication to the use of strophanthin. Cases with marked renal disease do not respond favorably to the use of strophanthin. A high blood pressure is not a contra-indication, but marked bradycardia always is. Stone gives the strophanthin in doses of 1 mg., which dose should not be repeated within twenty-four hours unless in exceptional cases.

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**Clinical Experiences with Calcium Lactate in Hemorrhages of the Upper Air Tract.**—SIMPSON (*Med. Record*, 1909, lxxvi, 505) writes favorably concerning the control of hemorrhage by the use of calcium lactate. His conclusions are as follows: (1) Clinical experience shows that calcium lactate has a controlling influence in hastening the coagulation of the blood. (2) Its efficacy is more marked in hemophilic cases in which the coagulation is delayed than in cases of normal coagulation time. (3) Before operation, especially on tonsils and adenoids, careful inquiry should be made relative to any hemophilic tendency. (4) In suspicious cases the coagulation period should be determined before operation. (5) It is questionable, if not positively contra-indicated, whether such operations should be undertaken in hemophilic cases other than under the most extreme urgency. (6) In all cases of operations for the removal of tonsils and adenoids, calcium lactate should be given for a period prior to and after the operation, both for its possible effect in diminishing the immediate hemorrhage and in preventing secondary surface hemorrhage. (7) Of the calcium salts, the lactate is more positive in its results, is more agreeable to administer, and is less irritating to the stomach.

**A Contribution to the Cause of Pernicious Anemia.**—BERGER and TSACIYA (*Deut. Arch. f. klin. Med.*, 1909, xcvi, 252) extracted with ether the mucous membrane of the gastro-intestinal tract of cases of pernicious anemia after death and obtained a lipoid substance which in vitro as well as experimentally on animals had a marked hemolytic action. The controls made with normal mucous membrane showed only a slight hemolytic action. They then produced a catarrhal inflammation of the gastric mucous membrane of dogs. The ether extracts of the involved mucous membrane contained a similar lipoid body. From these experiments they draw the conclusion that the cause of pernicious anemia is a chronic catarrh of the mucous membrane of the gastro-intestinal tract and the consequent production of a hemolytic substance. They explain the beneficial effects of intestinal lavage and diet in pernicious anemia upon this same etiological hypothesis.

## PEDIATRICS.

UNDER THE CHARGE OF

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**The Etiology of Epidemic Acute Anterior Poliomyelitis.**—P. H. ROEMER (*Münch. med. Woch.*, 1909, lvi, 2505) discusses the work done by him in determining the cause of anterior poliomyelitis. Microscopic and culture examinations of the pharyngeal and tonsillar secretions were entirely resultless; the same was true of the examinations of the cerebro-spinal fluid from six cases and of the brain and spinal cord of one child that died of the disease. Injections of the cerebrospinal fluid into mice, rabbits, and guinea-pigs remained negative; injections of an emulsion of the brain and spinal cord tissue into mice, guinea-pigs, and rabbits remained without result, but in the case of a monkey there occurred eight days after the operation a typical palsy and death. The histological examination of pieces of the nervous system of the monkey revealed typical changes of the disease. An emulsion made from the nervous tissues of this monkey and injected into rabbits produced no change, but when a monkey was used, the typical disease developed followed by death and changes typical of the disease. He concludes that the causal agent of epidemic acute anterior poliomyelitis most probably does not belong to a group of bacteria easily stained or cultivated—at least, it probably has never been either stained or cultivated. The virus is contained in the brain and spinal cord of individuals having the disease, and may be conveyed to monkeys by intracerebral inoculation. From cases of experimentally produced poliomyelitis in monkeys the virus can be conveyed to other monkeys by inoculation of brain or spinal cord emulsion. The possibility of an artificial cultivation of the virus in vivo is thus demonstrated.



**Henoch's Purpura or Angioneurotic Œdema.**—H. C. BARLOW (*Brit. med. Jour.*, 1910, i, 15) reports the case of a boy, aged twelve years, who with abdominal pain and diarrhœa, "the motions looking like blood," developed on both legs and hands white swellings the size of a walnut, which developed rapidly, lasted a few to twenty-four hours, and then disappeared. The bloody movements continued, the urine became bloody, and purpuric spots appeared, first over the elbows, later over other parts of the body. Improvement was followed by a return of symptoms in a similar routine; ultimately the boy recovered. A similar case is reported in a boy, aged four and one-half years. In this patient the condition lasted two months before convalescence became permanent. In neither case was the spleen palpable. In the first patient there was a slight elevation of temperature, and in both the pulse became slow and intermittent. In the second patient the joints were slightly involved. From being *in extremis* on one day, the second boy would return to apparently slight illness on the next. The best explanation for the illness, in the author's opinion, is a toxemia acting mainly on the sympathetic nervous system.

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**The Occurrence of Remissions and Recovery in Tuberculous Meningitis.**—The study of 797 cases of tuberculous meningitis occurring in seven London Hospitals since the year 1897, and of which 17 (2 per cent.), recovered, as well as a thorough study of such cases in the literature, have led A. E. MARTIN (*Brain*, 1909, xxxii, 209) to draw the following conclusions: (1) Undoubtedly long remissions and even recoveries do occur in tuberculous meningitis. (2) Recoveries are possibly more frequent than has been believed, since no fewer than twenty undoubted cases have been recorded since 1894, while other cases of recoveries have been reported in which the same definite proof of the nature of the disease has not been afforded, but some of which probably were true cases of tuberculous meningitis. (3) In those cases either the resistance of the individual is so much greater than usual, that the disease is checked early in its course, or the virulence of the bacilli is so much less than usual, that the lesion in the meninges becomes localized and later undergoes a fibrous change. (4) The lesion in the meninges may at a later period form the focus of a fresh infection, which usually terminates fatally, and consequently the prognosis in those cases must be guarded. (5) No treatment up to the present has been discovered which has had any specific effect in promoting the favorable termination of the disease.

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**Fifty-three Operations for Cleft Palate.**—C. HELBERG (*Berl. klin. Woch.*, 1909, xvi, 1757) relates his experience with operations for cleft palate, of which he has performed 53. He favors the performance of the operation in infants, having operated as early as the fourth month in healthy children. All of his patients (100 per cent.) recovered, and 40 (75.5 per cent.) were perfectly cured of their affliction; in eight there are fistulas remaining; a further attempt will be made to close them; in 5 the conditions are hopeless. The operation is no more difficult in very young children, if instruments of proportionate size are employed, than in older ones, and the earlier the operation is performed, the more likely is the patient of having a perfect functional result. Concerning

the technique, the author employs Langenbeek's method, but performs the operation like J. Wolff in two sittings. The first time the flap is loosened, the second time it is freshened and sutured. The dangers of flap necrosis are less, as the soft tissues can accustom themselves to the new blood supply. The flaps become thicker and broader and suturing is thus made easier. Hemorrhage is very slight if the sutures are put in some days after the loosening process. He employs silk for the soft palate and silver wire for the hard palate.

**Cerebral Hemorrhage in a Child.**—G. GHETTI (*Gazetta degli Ospedali*, 1909, xxx, 913) reports a case of cerebral hemorrhage in a boy, aged ten years. The boy was a foundling; at the age of eight a suprapubic cystotomy was performed for a vesical calculus; at the age of nine he had a rheumatic facial paralysis, and later headache was complained of for a long period, leading to a diagnosis of chronic meningitis. Ever since the bladder operation he had had some cystitis, at times there being difficulty in urination. On the night in question he retired in his usual health, sleeping normally until near midnight, when he rose to void urine. Shortly afterward the noise he made in breathing awoke the children, who slept in the same bed. He was unconscious and had a well-marked right-sided hemiplegia, the arm being in a state of semi-contraction. On the left side there was clonic convulsive movements. The right upper eyelid was lower than the left; the pupil reacted to light, not to accommodation. There was no knee-jerk on the right side, but there was a Babinski; on the left the reverse state was noted. There was incontinence of feces and urine. The child never recovered consciousness, and died on the fifth day. The autopsy showed a large hemorrhage in the left ventricle extending from the frontal to almost the occipital lobe. There was neither tumor nor tubercle; all other viscera were normal. The cerebral arteries were in a state of diffuse endarteritis. *Spirochaeta pallida*, in spite of close search, could not be found. The immediate cause of the hemorrhage was evidently the strain on urination, the bloodvessels being already diseased by a chronic degenerative process, probably syphilitic.

**Enterectomy under Spinal Anesthesia in an Infant Seven Months Old; Recovery.**—H. A. T. FAIRBANK and WILFRED VICKERS (*Lancet*, 1910, i, 364) report this case because of the rarity of recovery after enterectomy for irreducible intussusception in small infants, and also to emphasize the effect of spinal anesthesia on this type of case in children. There have been reported since 1906 but 3 or 4 successful cases of enterectomy in children under one year. The case in point was a female infant, aged seven months, with irreducible intussusception; temperature, 100°; pulse, 164; respirations, 36. A resection of the bowel was made, including the cecum, appendix, and a part of the colon. The operation was performed under spinal anesthesia, using Gray's stovaine, dextrin, and saline solution. A second injection of stovaine was given just before anastomosis was made, as the patient was beginning to show signs of shock—the effects of the first injection having begun to wear off. The authors believe that the spinal anesthesia saved the child's life, while chloroform anesthesia would have proved fatal. The toxic effects were reduced to a minimum

by using Gray's solution. Spinal anesthesia prevents shock from stimuli arising from the seat of the operation as long as the effects of the anesthetic continue. The pulse improved immediately after the injection. There was a more marked improvement of the condition after the second injection, which was given when the effects of the first injection began to wear off. The special advantage of this method is that it produces flaccidity of the bowel wall itself and facilitates reduction of the intussusception. Shock was conspicuous by its absence. Two other cases operated upon for the same condition showed similar results. Physiologically speaking, loss of tone in the muscular coats of the intestine is possible from high anesthesia. The child received three pints of saline solution daily by the rectum and subcutaneously for five days before nourishment was begun, with small doses of morphine. Spinal anesthesia cases show practically no shock. The Murphy button used in the operation passed in eighty-two hours. The toxic effects in spinal anesthesia are certainly less than with general anesthetics in desperate abdominal cases.

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## OBSTETRICS.

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**The Influence of a Bloodless Condition of the Uterus in Promoting Involution.**—LONGRIDGE (*Brit. Med. Jour.*, November 20, 1909) found upon investigation that in 150 primigravidae, during the latter months of pregnancy, blood pressure rose at term 20 mm. of mercury. After labor a corresponding drop is found, but even this leaves considerable pressure in the circulation. It seems to him reasonable that blood forced into the uterine wall at a pressure of over 100 mm. of mercury, would open vessels which are held closed during uterine relaxation only by elasticity of the muscle bundles. Yet we see cases after normal labor in which the uterus is relaxed, but does not bleed. There must be, in his view, some other provision of nature to prevent hemorrhage after labor. This he finds in the fact that when the uterus has expelled the child, it sinks down into the pelvis, carrying with it the uterine arteries, thereby shortening the length of the vessels two or three times. This produces numerous sharp kinks and twists in the vessels, which prevent the rapid flow of blood from the uterus, and are safeguards against hemorrhage. Anything which prevents the descent of the uterus, as the overdistention of the urinary bladder, will favor the occurrence of hemorrhage. He also calls attention to the fact that the healthy uterus loses half its weight in the first week by rapid autolysis. The mechanism of the circulation in the uterus is such that it is practically anemic after delivery, and is not continually flushed with an alkaline stream of blood. Autolysis of animal tissue takes place much more rapidly in an acid than in an alkaline medium. In order to test the correctness of

these observations, he examined puerperal patients for nitrogenous waste early in the puerperal period, examining the urine for creatinin. He found a marked rise about the end of the first week, which seemed to be the result of the retention of sarcolactic acid. Evidently the uterine muscle was undergoing rapid autolysis. He also refers to a case reported by Whitehead in the *British Medical Journal*, October 12, 1872. The patient was an anemic woman, who, after the birth of her last child, had postpartum hemorrhage. She did not have the ordinary lochia, but a discharge of a brown watery fluid, which persisted for two weeks without change in its appearance. Menstruation was never reëstablished, and on examination no trace of the uterus could be found; the entire organ had disappeared. This he explained by the rapid autolysis of the uterine muscle, from the pronounced anemia present, the acid condition of the uterus, and the absence of alkaline blood. Clinical observation has shown that patients are sometimes free from lochia with the exception of a slight mucoserous discharge. In these cases after the fifth or sixth day, a very slight reddish discharge has been noticed, which soon ceases. This probably occurred when the circulation of the uterus was reëstablished. It is quite possible for patients to pass through the puerperal period without lochial discharge and to have rapid and complete involution. In the case of other warm-blooded animals than human, recovery after parturition is not accompanied by the pretence of a lochial discharge.

**Adrenalin in Pernicious Nausea of Pregnancy.**—REBAUDI (*Zent. f. Gynäk.*, 1909, No. 44) narrates a case in Bossi's clinic at Genoa in which a primipara suffered from general indisposition, asthenia, melancholy, and depression. The patient had many symptoms of toxemia, headache, vasomotor disturbance, loss of appetite, impaired digestion, and excessive secretion of saliva. Pernicious nausea afterward developed. Various methods of treatment were unsuccessful, and the interruption of pregnancy was seriously considered. Before resorting to this the patient was fed by rectal injections, and 20 drops of 1 to 1000 adrenalin were given daily, 10 in the morning and 10 in the evening. During the first three days the patient also received by rectum a small quantity of water containing 20 drops of laudanum, and after that small doses of ice water. In about two days after beginning this treatment the vomiting, which had been practically continuous, ceased, and on the third day the patient took small quantities of cold food. The symptoms had so largely disappeared by the sixth day that the patient felt comfortable. On the eleventh day the dose of adrenalin was reduced to 10 drops, and this was continued for nine days. The patient's condition became practically normal, she was able to take nourishment and gained in weight, and the ovum grew in a normal manner. Later the patient had a recurrence of the nausea and other symptoms, which ceased after five administrations of 10 drops of the solution daily. The fact that the patient was fed by the rectum, and given small doses of opium by the same method, makes it doubtful whether the adrenalin was the potent agent in the patient's recovery. So many of these cases improve if life can be supported for a few weeks that it is difficult to decide that adrenalin alone was the potent agent in the patient's recovery.

**The Surgical Treatment of Puerperal Sepsis.**—KOBLANCK (*Zentralbl. f. Gynäk.*, No. 46, 1909) gives the results of treatment in 484 cases of puerperal sepsis, of whom 100 had severe infection. It was impossible to divide these cases into typical septicemia and pyemia. In 34 cases treatment was satisfactorily carried out by collargol.

Puerperal septic peritonitis was observed in three varieties: One followed perforation, the active agent being *Bacillus coli communis*, with symptoms of pronounced distention and great tenderness of the abdomen.

These cases gave a fairly good prognosis if operation was quickly performed. One of these patients treated by abdominal total extirpation of the uterus recovered; two others not operated upon died.

The second variety of infection was that which developed gradually with the formation of encapsulated pus. The rapidly increasing leukocytosis was significant in forming the diagnosis. In many of these patients the abdomen was not distended, nor especially painful. Of the three cases operated upon, one of these recovered.

The third variety of sepsis could be entitled the fulminant sort in which the infection arose usually through the genital organs, and rarely from a focus without the genital tract. In these cases not only must the peritonitis be treated, but the infected condition of the uterus also demands attention.

In five of these patients operated upon, one recovered. One of these patients suffered from angina in addition to the septic infection.

In operating upon these cases, not only must the abdomen be opened for drainage, but the operator must separate adherent intestines and omentum, wash out or sponge out the pus, make counter openings, and irrigate through these openings for complete drainage. Good results were obtained by continuous irrigation with warm salt solution through the openings for drainage.

In treating suppurating thrombophlebitis it is important to diagnose the condition as early as possible. The diagnosis is made more certain by reference to the leukocyte count, which in these cases approaches more nearly the normal than in cases of parametritis and peritonitis. Ligation of the thrombosed veins and broad ligaments seems to influence the course of the disease in four ways—it prevents the extension of the thrombus to the vena cava, prevents the distribution of minute thrombi through the circulation, limits the infection to the uterus, and prevents the spread of bacteria.

Koblanek does not think it sufficient to simply ligate the veins, but believes it necessary to remove purulent foci as well. This was performed in 6 cases of extirpated thrombosed veins, removing as much as possible of the infected parametrium, tubes, and ovaries, and the infected tissue of the uterus as well. Two of these patients recovered.

This operation is indicated only in those cases in which the body of the uterus seems to be healthy. Unless this is the case the uterus must be extirpated. In 3 fatal cases autopsy showed that the leaving of the uterus had been a mistake.

In 15 cases the extirpation of the septic uterus was practised, with 6 recoveries, and 9 deaths.

Indications for operation were uterine infection with hemolytic streptococci. Contra-indications for the operation were metastases in

the heart, lungs, and eyes, as in these cases recovery is exceptional. In 19 patients having septic lesions of the heart, but 2 recovered; in 8 septic cases with ocular complications, but 1 recovered; in 55 septic cases with septic lesions of the lungs or pleuræ, but 9 recovered. The general resisting power of the patient is of great importance in these cases.

Cases operated upon by total extirpation were divided into those where general infection was present, and those patients in whom the first symptoms of general infection were discernible.

In the first class, 11 operations were performed, and of these, 2 had general peritonitis, 5 thrombophlebitis with phlegmonous inflammation of the pelvic connective tissue, 3 parametritis and abscess in the broad ligament, while 1 had general septic infection without a clearly defined localized focus, but with abundant streptococci in the blood. Of these 11 patients, but 3 recovered.

In the second group there were 4 cases—3 in which the infection seemed to be limited to the uterus, and 1 with general peritonitis, apparently spreading from the uterus. All of these recovered.

In these cases it may be impossible to say that the patient would not have recovered without operation in some.

Vaginal extirpation may be chosen in threatened general infection where the uterus at the time of operation seems to be the principal focus. In all other cases abdominal section must be practised and the operation suited to the lesions which are found.

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## GYNECOLOGY.

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UNDER THE CHARGE OF

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**The Surgical Treatment of a Most Frequent Cause of Dysmenorrhœa and Sterility in Women.**—S. Pozzi (*Surg., Gyn., and Obst.*, 1909, ix, 111) described to the American Gynecological Society an operation he has devised for dysmenorrhœa and sterility in women. The operation is limited to nulliparous women suffering from "cervical metritis due to stenosis." Pozzi terms the operation "stomatoplasty by commissural evidentment." The technique of the operation is thus briefly described: The cervix is exposed and grasped anteriorly and posteriorly by bullet forceps. It is next dilated by Hegar's dilators up to number 20 or 30; after bilateral discission of it to a distance of 2 or 3 c.m., curettage with an intra-uterine aseptic flushing is followed by an injection of perchloride of iron, and that by another aseptic injection. Then comes the principal part of the operation. A navicular piece of tissue is next removed from each lateral denuded surface and the cervical mucosa and vaginal surface are united over the excavation by interrupted sutures,

while the anterior and posterior flaps are widely separated. The denuded surfaces closely resemble those denuded from trachelorrhaphy, but the flaps are kept apart instead of being sutured together. The middle suture at the bottom of each sulcus is the first one tied. Pozzi claims splendid results from this procedure.

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**The Mechanism of Occlusion of the Fallopian Tube.**—EMIL RIES (*Amer. Jour. Obst.*, 1909, lx, 201) commented at length on the literature of this subject and presented two illustrative specimens to the Chicago Gynecological Society. He declares there is very satisfactory argument as to the actual observations of this condition, but that differences arise in the interpretation of these facts, the main difficulty arising over the mechanism which causes the fimbriated ends to turn from their normal condition to that found in occlusion, a turn of apparently 180 degrees. Ries suggests that the peritoneum surrounding the fimbriae becomes inflamed and contracts, forming a non-elastic ring. The subsequent distention of the tube, followed by relaxation incident to absorption of its contents, permits the ring to contract further. The fimbriae, being covered by epithelium, do not adhere to the ring and escape inwardly.

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**Chronic Inversion of the Uterus.**—SEALY (*Amer. Jour. Obst.*, 1909, lx, 284) records a case of inversion of the uterus for two years and four months duration cured by posterior colpotomy and posterior uterine section. The cervix was first medially split posteriorly, and then the peritoneum was opened. The uterine incision was by gradation finally extended to the fundus, as taxis failed to produce reduction with shorter ones. A finger introduced from behind into the abnormal uterine cavity was a valuable guide. Sealy claims for this method of procedure that it is easy, comparatively safe, and absolutely successful regarding reduction of the inversion.

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**Suprapubic Operation upon the Pelvic Floor for Prolapse of the Uterus.**—W. M. POLK (*Amer. Jour. Obst.*, 1909, lx, 418) recommends for extreme prolapse of the uterus and bladder the following procedure: After a limited preliminary treatment, including rest in bed, to improve the local and general condition of the patient, the usual median line incision is made through the lower abdominal wall and the patient's position changed to that of Trendelenburg. The pelvis is carefully emptied of omentum and intestines, except the sigmoid and rectum. With a tenaculum the uterus is grasped at its junction with the anterior peritoneal reflection and traction made; the bladder is drawn well forward and an incision is made in the median line from the tenaculum forward and downward to the urethra and the vaginal wall without opening the latter. Avoiding the ureters and uterine arteries as well as the vagina, the fascia is brought in toward the median line by means of one tier of continuous deep suturing; another layer of similar suturing draws in all slack tissue on either side. The uterosacrals are shortened next. The abdomen is now closed. If the uterus should be amputated, it is done at the level of the internal os before the anterior incision is made, and the stumps of the broad and round ligaments are subsequently sutured to the top of the cervix and the uterosacrals sutured over on

top of them, perhaps crossing each other. In some instances in which the uterus is to be retained the round ligaments may need shortening. Rectocele and peritoneal lacerations may be then or later properly treated.

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**Fever in Cases of Myoma Uteri.**—OTTO V. FRANQUE (*Ztschr. f. Geburtsh. u. Gynäkol.*, 1909, lxiv, Heft 3, 449) has observed the occurrence of fever in many cases of uterine myomas which could be attributed to (1) an aseptic necrosis of the tumor, (2) a bacterial infection of the growth by way of the blood stream, (3) thrombosis and phlebitis, and (4) a coincident salpingitis. In such cases the fever may be the only indication of a complication, and therefore clinical observations for several days should always precede severe operations for myomas. He holds that complete necrosis of myomas during pregnancy is much more common than heretofore believed, and that as such conditions are very favorable to local infection, the occurrence of fever during the puerperium in cases of uterine myomas should suggest an early operation to prevent the appearance of severe septic symptoms.

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**Extension of Uterine Adenomyomas to the Rectum.**—ANTON SITZENFREY (*Ztschr. f. Geburt. u. Gynäkol.*, 1909, lxiv, Heft 3, 538) has studied four cases of involvement of the rectum by so-called adenomyomas of the uterus, and from his own observations and a review of the literature concludes that genuine adenomyomas very rarely extend from the uterus to the rectum. He believes that growths involving both organs are, as a rule, adenomas with an accompanying myositis of the rectum rather than true adenomyomas, though he considers it possible for the adenoma element to extend from the uterus to the rectum and there set up an inflammatory reaction, which in turn may result in the development of a true adenomyoma, the myoma element being derived from muscular tissue of the rectum. The distinction between an inflammatory infiltration of the rectum and the presence of a tumor is of great importance from the standpoint of operation, as in the first case the removal of the primary growth in the uterus causes a disappearance of the enlargement in the rectum, while in the latter case a resection of the rectum is indicated. In many cases it is not possible to distinguish at the time of operation between adenomyoma or adenomyositis and carcinoma.

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**What is the Preferable Time for Abdominal Operation for a Chronic Inflammatory Mass in the Pelvis.**—H. S. CROSSEN (*Surg., Gyn., and Obst.*, 1909, ix, 405) states that in more than half of the cases of chronic suppuration in the pelvis the pus is sterile at the time of operation, showing that sterilization of the infected focus takes place automatically within a reasonable time in the majority of cases. Crossen emphasizes the markedly greater safety in the abdominal removal of the mass after, instead of before, the death of the bacteria. He cautions against abdominal operations for such conditions caused by the streptococcus, even though the pulse and temperature have become normal. It is especially recommended that the variety of infecting organism be learned, if possible, before operation. For determining this point good working rules are given.



**Final Word on the Stem Pessary for Amenorrhœa, Dysmenorrhœa, Sterility, Etc.**—J. H. CARSTENS (*Jour. Amer. Med. Assoc.*, 1909, liii, 1730) has written a fourth paper on the subject of the use of the stem pessary for various uterine functional abnormalities. For amenorrhœa, premature atrophy, dysmenorrhœa, displacements of the uterus, and sterility He strongly recommends the application of the stem pessary. In some instances its retention for one to two years is advised. He regards pelvic inflammations as contra-indicating the use of the stem pessary.

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## DERMATOLOGY.

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**Lupus or Tertiary Syphilis? Sarcoma or Primary Syphilis?**—Under this heading A. NEISSER (*Berl. klin. Woch.*, August 16, 1909) discusses the differential diagnosis, giving the notes of a case of supposed lupus in which existing syphilis was not diagnosticated for two years. When there exists a suspicion of syphilis, he advises energetic mercurial and iodide treatment. Nasal disease first manifesting itself in a woman as late as the age of forty-one is more likely to be syphilis than lupus. A negative history, especially in women, does not exclude syphilis. The author advises the employment of the subcutaneous tuberculin test in all instances of a superficial disease suspected of being tuberculosis. A case is cited in which a large red warty patch had been observed for two years on a young man and the diagnosis of tuberculosis verrucosa made, but no reaction followed tuberculin up to 5 mg., but the Wasserman test proved that syphilis existed, and recovery followed the usual internal remedies. A case is referred to in which a woman was believed to have a sarcoma of the uterus, the microscopic examination pointing to that disease, and hysterectomy was performed. Later, a papular syphiloderm appeared. The Wassermann test before the operation would have indicated the necessity for an antisyphilitic treatment.

**Experimental Studies Concerning Tuberculosis of the Skin.**—LEWANDOWSKY (*Archiv f. Dermat. und Syph.*, 1909, xcvi, Heft 2 and 3), who has made a somewhat extensive study of the results following the inoculation of human and bovine tubercle bacilli into the skin of rabbits and guinea-pigs, has found that such inoculation when properly performed always leads to a local tuberculosis of the skin. The result of the inoculation is dependent upon the varying virulence of the strain of the bacilli employed and upon racial and individual differences of the

animals inoculated. The typical inoculation ulcer appears in guinea-pigs only in the second week, and may last until the death of the animal or it may heal over. In the latter event the small red-brown discolored spot remaining still contains tuberculous tissue and is inoculable. Tuberculosis of the lymph cords only appears after the lymph-glands in the neighborhood are affected, and this may lead to the formation of nodules with crateriform ulcers which only heal in the last days of the animal's life. In rabbits, in addition to ulcers, inoculation produces foci similar to lupus or, according to location, tuberculosis verrucosa. Intravenous injections into the engorged ear of the rabbit may produce a papular eruption on the skin of the ear, which undergoes spontaneous involution and contains bacilli only in the beginning (tuberculide-like lesions). After similar injections with bovine bacilli a true tuberculosis occurs. Infection of the skin with bovine bacilli leads in rabbits always to general tuberculosis, but infection with human bacilli pursues a different course; even intravenous injection is not always followed by general tuberculosis. Of internal organs, the lungs are almost always affected in rabbits after cutaneous infection. Histologically caseation is almost always wanting in the skin. In animals which have undergone a cutaneous inoculation, subsequent inoculations, if they are made some time after the first one, take effect less vigorously than the first, unless the later ones are made with bovine bacilli. This relative immunity of the skin also appears after intraperitoneal inoculation.

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**Dermatitis Herpetiformis.**—BOGROW (*Archiv f. Dermat. und Syph.*, 1909, xcviii, Heft 2 and 3) reports a case of dermatitis herpetiformis with extensive eruption which, beginning acutely in a woman with carcinoma uteri, began to undergo regression coincidently with the employment of disinfecting vaginal douches, the internal administration of calcium chloride, and the local use of astringent salves and compresses. An abrupt ending of the cutaneous affection and fall in the elevated temperature followed immediately upon an operation in which the entire visible, partly necrotic mass of the tumor was removed. Recurrence of the growth, which caused the death of the patient, was not followed by a return of the eruption. The author regards the case as a toxidermia proceeding from the necrotic tumor of the uterus, from which bacterial products reached the circulation, a view which the results of treatment support. Should future observations of a similar nature be made, the author believes they would furnish ground for more closely associating dermatitis herpetiformis and impetigo herpetiformis.

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**The Treatment of Itching Dermatoses, Especially Trade Eczema, with Undiluted Coal Tar.**—CHAJES (*Dermat. Ztschr.*, 1909, xvi, Heft 9), who has employed coal tar in the treatment of 64 cases of various diseases of the skin, such as eczema, lichen planus, prurigo, and pruritus hiemalis, finds that it is an excellent and quickly acting remedy in many acute and chronic itching affections, being especially valuable in the treatment of those eczemas occurring in workers in various trades. It lessens itching, diminishes redness and swelling, and dries up and heals oozing eczemas. It is contra-indicated in infection of the skin, since suppuration can take place and spread under the coal tar. The method of application is quite

simple, consisting in applying a moderately thick layer of the tar to the affected area with a not too stiff brush, previous cleaning being necessary only in those cases attended by abundant exudation and the consequent formation of thick crusts.

## PATHOLOGY AND BACTERIOLOGY.

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**The Action of Leukocytic Extracts on the Course of Pneumonia.**—The idea that leukocytes contain substances which, when present in a free state, might have a beneficial effect upon infectious processes originated with Hiss. His hypothesis was that the phagocytic cells contain an anti-endotoxin which protected the cells against the endotoxins of the bacteria which had been ingested. If this anti-endotoxin was liberated in a free state it would have a beneficial effect in the animal suffering from an infective process. This hypothesis was put to extensive experimental investigation by HISS and ZINSSER (*Jour. Med. Research*, 1908, xix, 323) by injections of leukocytic extracts into animals after they had been inoculated with various pathogenic bacteria. This procedure gave such good results in effecting favorably the course of the infections in animals that it seemed justified to use the method as a means of treatment in human infectious processes. This method has been used in man by Hiss and Zinsser, who have made, besides their original report, a second one on the treatment of staphylococcus infections with leukocytic extract (*Jour. Med. Research*, 1909, xx, 506). It has also been employed by LAMBERT (*AMER. JOUR. MED. SCI.*, 1909, cxxxvi, 506) in a variety of infectious processes in man. But the most extensive employment of this method of treatment in any one disease is that reported by FLOYD and LUCAS (*Jour. Med. Research*, 1909, xxi, 223), who used leukocytic extract as a method of treatment in 41 cases of pneumonia. Leukocytes were obtained from young rabbits after injections into the pleural and abdominal cavities of 10 c.c. of a 5 per cent. aleuronat solution. The exudate thus obtained was washed and centrifuged, the leukocytes were broken up by beating with a platinum loop, and extracted with distilled water. Ten c.c. subcutaneously injected twice a day was the standard dose. As much as 20 c.c. three or four times a day was given without any harmful effects. There were five deaths in these cases, giving a mortality of 12.5 per cent., which is to be contrasted with a mortality of 21 per cent. occurring in cases of pneumonia treated by other methods under the same general conditions. All of the cases treated were lobar in type except three, which were cases of bronchopneumonia. Of the 5 cases that died, 2 were

of bronchopneumonia in children. Of the 3 fatal adult cases of lobar pneumonia, 2 had heart lesions and 1 was a man aged seventy years. What seems to be the most striking result is, however, that in 44 per cent. of the treated cases the crisis occurred on or before the sixth day. No bad effects were seen, and the benefit obtained from the treatment is strikingly seen when some of the individual cases are considered.

**The Diagnosis of Cancer of the Stomach by Salomon's Test and by the Hemolysin Method.**—In 1903 SALOMON (*Deut. med. Woch.*, 1903, xxxi) published a test for the diagnosis of cancer of the stomach based on the fact that due to the carcinomatous degenerated stomach wall the stomach washings of such cases contained more albumin than those of normal stomachs. The procedure consists in washing out the stomach the evening before the test, and then washing it again in the morning with 400 c.c. of normal salt solution. From 100 c.c. of this wash water the nitrogen content is estimated by the Kjeldahl method and the albumin with Esbach's reagent. A result of more than 20 mg. of nitrogen and a cloudy Esbach reaction are considered to point strongly toward carcinoma, though the results are vitiated if there is excessive mucus present. This can be prevented by previously separating the mucus out by acetic acid. Non-ulcerating carcinomas may also give negative results; and positive results may be obtained in non-carcinomatous cases if the stomach is primarily not completely washed out or if there is ulceration from other causes. Reicher showed that the nitrogen came from the nucleo-albumin of the tumor cells rather than serum-albumin, and recently GOODMAN (*Univ. of Penna. Med. Bull.*, May, 1909) has found that the phosphates in the stomach washings of carcinomatous cases usually exceeded 10 mg. per 100 c.c., while in non-carcinomatous cases they were below 10 mg.

Last year GRAFE and ROHMER (*Deut. Archiv f. klin. Med.*, 1909, xciii, 161) elaborated another method depending on the presence of lipid substances in the carcinomatous stomach wall, which can be demonstrated in the stomach contents by their strong hemolytic action. The technique is as follows: The fasting stomach is washed and emptied, and a test meal given. The filtrate of the stomach contents obtained one hour after the test meal is made faintly alkaline to litmus and an equal amount of ether is added. It is shaken for twelve hours and the ethereal extract removed and evaporated. The residue is then so emulsified in normal salt solution, that 1 c.c. of the salt solution represents 10 c.c. of the stomach contents. It is added to an equal amount of a 5 per cent. mixture of freshly washed rabbit corpuscles, and brought up to 3 c.c. with salt solution. After three hours in the thermostat, shaking up once or twice, it is left in the ice chest over night. Only those stomach contents should be considered positive in which there is complete hemolysis, a brownish discoloration denoting an insufficient amount of alkali.

ROSE (*Deut. Arch. f. klin. Med.*, 1909, xcv, 518) has compared the two methods in 37 cases, with the following results: In 8 cases of certain carcinoma both tests were positive; in 22 cases other than carcinoma both tests were negative. In one case of extreme gastropnoia both tests were positive, the Salomon test because of mucus and bile in the stomach contents, the hemolysin because of the backflow of the

pancreatic juice. In one case of ulcer of the stomach in which there had been a hemorrhage within a month, the hemolysin test was positive, the Salomon negative. In one that subsequently proved to be a carcinoma of the gall-bladder, the Salomon test was positive, the hemolysin negative. Rose believes that in cases in which there is an extensive ulceration a negative Salomon test points to a benign ulcer, even if the hemolysin test is faintly positive. In gastropexia, which seems to be the commonest source of error, a positive hemolysin test with a negative trypsin content admits of a diagnosis of malignancy. Rose considers both tests to be equally valuable, though from neither can an absolutely certain diagnosis be made.

**Hemolytic Jaundice.**—MARCHIAFAVA and NAZZARI (*Bull. della Reale Acad. Med. di Roma*, Fasc. 3, 1909) divide cases of hemolytic jaundice into those running acute and chronic courses. Examples of the former occur in poisoning by hemolytic substances and in malaria, whether simple or complicated by hemoglobinuria. In these forms of jaundice the feces are deeply colored, bile pigment is often lacking in the urine, which may contain urobilin or hemoglobin, and microscopically, granular casts or masses of hemoglobin and epithelial casts with protoplasm stained with hemoglobin. At autopsy, the liver is enlarged, congested, rich in bile; while the gall-bladder is turgid with thick, dark bile and the duodenum is bile-stained. Microscopically, the liver cells do not show greater changes than in other malarial infections. The epithelium of the renal tubules is infiltrated with hemoglobin or pale yellow granules. The hemolytic jaundice with a chronic course may be either acquired or congenital. The congenital form is less severe, and in them the icterus outweighs the anemia. In the more severe acquired forms the anemia outweighs the icterus, and the patient presents the picture of pernicious anemia. From observation of a typical case of each kind and a survey of others reported in the literature, Marchiafava and Nazzari offer the following facts in favor of the hemolytic origin of the jaundice: the anatomical integrity of the liver accompanied by a polychromic polycholia (observed intra vitam during operation for cholecystostomy); the progressive diminution of the number of red blood cells; the almost continuous elimination in the urine of blood pigment in solid form, with crises of hemoglobinuria and urobilinuria, the presence in the blood cells of the granules of degeneration; finally the analogy with the symptoms of other hemolytic affections, whether spontaneous (as idiopathic or malarial hemoglobinuria) or provoked experimentally in animals by means of hemolytic poisons.

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ORIGINAL ARTICLES.

VACCINE THERAPY IN COLON-BACILLUS INFECTION OF  
THE URINARY TRACT.<sup>1</sup>

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COLON bacilluria occurs in fully 50 per cent. of all cases of bacteriuria. The condition may be unattended with perceptible effect, either local or systemic. Patients may suffer from dysuria with frequent urination and the colon bacilluria may be the only recognized morbid condition. Usually the bladder irritation is ascribed to the hyperacid urine, but it may continue when the urine is rendered alkaline. That the colon infection is the chief cause of the bladder irritation is presumptively proved by the relief of all symptoms coincident with the disappearance of the bacteria from the urine.

Colon bacilluria may be present with recognizable morbid changes in the urinary tract; the bacteria are either the cause or are closely related to the disease process. The morbid anatomical change, probably, frequently preëxists in the mucous membrane of some portion of the urinary tract. The urethra, prostate, ureter, kidney pelvis, and kidney may be involved. A urinary calculus may preëxist and also may result from a colon bacilluria. Colon urinary infection may be present with tuberculosis of the urinary tract and apparently aggravates the associated morbid anatomy, and intensifies the disturbance of the urinary apparatus and the general symptoms. It may also rarely be present with and aggravate the local disturbance and general symptoms of gonococcic infection of the deeper urinary

<sup>1</sup> Read at a meeting of the Medical Society of the State of New York, January 26, 1910.  
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tract; of pyogenic streptococcic and staphylococcic, proteus, influenzal, typhoid-bacillus, and other bacterial infections of the bladder and kidney pelvis. Prostatitis, cystitis, ureteritis, pyelitis, and pyelonephritis may occur with colon bacilluria alone and as a mixed infection, especially in tuberculosis of the urinary tract. Chronic arthritis, myocardial degeneration, myalgias, and various other systemic conditions apparently may be related to the urinary infection.

**MODE OF ENTRANCE OF COLON BACILLI INTO THE URINARY TRACT.** This may be through the urethra in the female with or without instrumentation, and in the male probably only by instrumentation. The prevalence of colon bacilluria in people who have never had a catheter or sound passed into the ureter, proves the existence of other routes of infection. In the vast majority of patients the source is unquestionably the gastro-intestinal tract. Obstinate constipation or diarrhea, attended with more or less injury of the intestinal mucosa, renders the intestinal wall previous to the bacteria, which may then be carried by the blood or lymph stream to the kidney, ureter, and bladder. Colon bacilli from this source have been proved to take on more virulent characteristics.

The diagnosis of bacteriuria is easily made by microscopic examination. The character of the bacteria usually requires a cultural examination of the urine. From a, preferably catheterized, specimen, primary plate cultures should be made; the final recognition of the bacterium by subcultural and tinctorial tests is a common laboratory procedure. A careful physical examination of the patient, with chemical and microscopic study of the urine, will enable one usually to make an anatomical diagnosis. One should never fail to make a careful examination of the external genitals of the patient, both male and female, for focal infection. The rectum should also be inspected. The prostate should be palpated, and possible sacculation of the bladder by abnormal deviations of the uterus and by a lax vaginal wall should be investigated. If indicated, a cystoscopic examination and catheterization of the ureters should be made. The greatest care must be exercised to catheterize the ureters. This is especially true when the bladder is badly infected. The anatomical diagnosis is most important from the therapeutic point of view. If a morbid condition of tissue exist which interferes with the function of the urinary apparatus, no permanent benefit will result from medical treatment, until as nearly as possible a normal anatomical condition is brought about. Colon bacilluria may not be removed as long as poor drainage of the urinary tract exists because of sacculation of the bladder, enlarged prostate, stricture, pressure obstruction, or kink of the ureter, kidney-pelvis sacculation, or if a calculus or other foreign body be present.

Formerly the recognized treatment of colon bacilluria consisted preferably in prolonged rest in bed, a copious liquid diet of milk,

soups, broths, etc., and the use of urinary antiseptics—of which hexamethylenamine is the best. By this method treatment was long, extended to months, and the result was often poor. For the last five years in the medical clinic of Rush Medical College associated with the medical wards of the Presbyterian Hospital and the laboratory of the Memorial Institute for Infectious Diseases, bacteriuria has been carefully studied and many patients have been treated with autogenous vaccines. The work has been carried on by the clinical department of the college and hospital. I have received most valuable coöperation and aid from my colleagues and assistants. The bacterial cultures and autogenous vaccines have been made chiefly by Dr. D. J. Davis,<sup>2</sup> of the medical department, and now an assistant in the Memorial Institute for Infectious Diseases.

When possible the agglutination, opsonic index, bacteriolysis, and the leukocytic blood reaction were studied in each patient. The observation of other reporters as to the character of the bacteriuria has been confirmed. Those suffering from infection of the urinary tract due to the colon organism comprise more than 50 per cent. of the patients with urinary infection. Frequently the gonococcus was obtained with the colon infection from the prostate or seminal vesicles by stripping those organs with the finger in the rectum. Undefined bacteria were sometimes found with the colon; occasionally the unknown organism would be obtained only in plate cultures, failing to grow in anërobic or aërobic subcultures. In some instances the unknown bacterium persisted in the urine after the colon bacillus had disappeared and the patient was symptom-free.

Colon-bacillus infection with tuberculosis of the urinary tract occurred in two patients; the great discomfort occasioned by bladder pain, frequent urination, and septic fever was almost entirely relieved by the disappearance of the colon infection after autogenous vaccination. Two patients suffering from essential hematuria with colon infection have been treated by vaccination. In one, a woman aged twenty-four years, intermittent hematuria had existed for six years or more. A moderate pyuria existed. Repeated examination of the urinary sediment failed to reveal tubercle bacilli. Animal inoculation with the urinary sediment was negative. The ophthalmo-tuberculin test was negative. Cystoscopic examination revealed a normal bladder mucosa. The ureteral catheter entered the right ureter with difficulty and the drop by drop fluid obtained contained blood, leukocytes, and colon bacilli. The left ureter was normal and the freely flowing urine was practically normal. In June, 1907, a right nephrotomy was made; the urine from the kidney pelvis contained red cells and leukocytes and

<sup>2</sup> See report by Dr. David John Davis, "Immune Bodies in Urinary Infections with Colon Bacilli and Treatment by Inoculation," *Journal of Infectious Diseases*, 1909, vi, 224.

the colon bacillus. The mucosa of the pelvis was thickened and congested. The kidney capsule stripped off normally and a section of the cortex showed histologically interstitial diffuse nephritis. The kidney pelvis was packed with gauze and later was daily injected with argyrol solution, which penetrated to the bladder. Hemorrhages recurred before the external wound had healed and afterward. Six months later, in January, 1908, the patient was again taken into the hospital and injections of autogenous colon vaccines were given every seven to ten days until April, 1908. Hemorrhage ceased. Since that time the urine is blood-free except for a few red cells in the centrifuged sediment. No urinary symptoms remain.

A physician of fifty-eight who always has enjoyed good health, suffered from hematuria without pain in August, 1909. In October cystoscopy revealed a normal bladder mucosa, bloody urine flowing from the right ureteral orifice, and normal urine from the left ureter. Ureteral catheterization was negative for obstruction or stone and the x-rays also were negative. Probable tumor of the kidney was diagnosticated. Later he was admitted to the Presbyterian Hospital. The physical examination revealed a good general condition. The urine contained much free blood, many leukocytes, no casts, and was acid in reaction. A pure culture of colon bacilli was obtained from the urine. A milky fluid obtained by stripping the prostate showed many pus cells and a few Gram-negative intracellular biscuit-shaped diplococci. The prostate was stripped every three or four days until no discharge was obtained. The patient was treated with the autogenous colon vaccine every seven days. The blood disappeared from the urine after the third vaccination. The urine remains blood-free and the patient is apparently well.

In September 19, 1908, a physician, aged twenty-nine years, was seized with anuria, and uremic convulsions, which were partially relieved the first day. Headache, vomiting, occasional mild convulsions continued for six days. The scant urine contained a good deal of pus, but no casts or blood. October 21, 1908, he was admitted to the Presbyterian Hospital. The general examination revealed no perceptible morbid condition of heart, bloodvessels, lungs, or abdominal organs. The arterial tension was 120 mm. The eye-grounds were normal. The urine was acid, contained many polynuclear leukocytes (60 per c.mm. of urine), no casts, no red cells, and a trace of nuclealbumin. Many bacilli were seen and a pure culture of colon bacilli was obtained. The history revealed the probability that the colon infection of the bladder had existed for five years. During that time albuminuria was present for two years and thereafter occasionally only. A month preceding the convulsions he was conscious of lessened strength and endurance, dull headaches, anorexia, and lessened excretion of urine. Autogenous colon vaccination was begun with 400,000,000 bacteria on November 11, 1908. These were repeated every seven to ten days until December 11, 1908, at which

time the urine was almost free of bacteria and pus cells. The patient continued the treatment at home. On March 23, 1909, the urine was sterile and pus-free. The patient has had no relapse.

A man aged thirty-one years, suffering from tuberculosis of the urinary tract which began in the right testis in 1903, was admitted to the Presbyterian Hospital in October, 1907. The right testis had been removed in 1903 and a right nephrotomy and curettage of the kidney pelvis was done in June, 1907. The patient was suffering greatly, although constantly narcotized with opium. There was a septic temperature. No perceptible evidence of tuberculosis of lungs or lymph glands was present. The urine was very cloudy and discolored with abundant pus, blood, and bacteria. Tubercle bacilli were abundant in the urine sediment. Per rectum a nodule in the right lobe of the prostate was tender. The right ureter could be felt as a thick tube, and this and the resistant bladder wall were very tender. From the urine was obtained a pure culture of the colon bacillus. The patient was given absolute rest in bed, and received tuberculin (N.T.), 0.001 mg., every seven or eight days and coincidentally therewith was vaccinated with 500,000,000 autogenous colon bacilli. With the third injection the urine became colon-free. Coincidentally the urine became much clearer, containing less pus and blood. The frequency of urination lessened from every one-fourth to one-half hour to as long as three or four hours. The general condition improved by the disappearance of fever and sweats and the appetite returned. Opiates were discarded. The patient left the hospital in December, 1907, and has remained on a farm. He has continued to use the injections of (N.T.) tuberculin, 0.001 mg., every seven to ten days. Examination of the urine every six months reveals the presence of a few leukocytes, red cells, and small clumps of tubercle bacilli. The bladder irritation is not severe and the general health is good. Probably recovery would occur if the patient could take prolonged rest.

These case reports suffice to illustrate the utility of colon vaccine therapy. In a later paper on vaccine therapy in bacteriuria a detailed tabulated report will be made. Patients suffering with pyelitis with colon bacillus infection have recovered with autogenous vaccination when there was no obstruction to drainage. Improvement may occur under the treatment in all cases, but entire recovery from the colon bacilluria will usually not occur if there is stagnation anywhere in the urinary tract. If the enlarged prostate is at fault, rational massage of that organ may be all that is necessary. If there be deformity of the pelvic organs or distortion of the kidney pelvis, or the existence of a urinary calculus, surgical interference should be instituted.

Systemic effects of urinary focal infection must not be overlooked. A chronic infectious arthritis, myocardial degeneration, so-called chronic muscular rheumatism, and neuritis may be related to the

urinary infection. The resistant epithelial layer of the urinary tract probably prevents toxemia until long continuation of the infection causes injury of the epithelial layers and then absorption of toxins may occur.

The bacillus isolated from cases of colon bacilluria differ from each other more or less in size, luxuriance of growth, etc. It would seem rational, therefore, to use autogenous vaccines. This is easily done. Cultures may be made from the urine after it has been transported a thousand miles to a laboratory, by one properly trained in bacteriological technique. We have had no experience with commercial stock vaccines and no comparison may be made of them here.

The autogenous vaccine may be made by heating the culture to 60° C. for thirty minutes. This has proved to kill the bacilli, as shown by control cultures. Fresh suspensions of the dead bacilli should be used. Suspensions more than two weeks old may not give the same results. Usually the first vaccination is made with 200,000,000 bacilli. The subsequent dosage may be gradually increased until a decided local and general reaction occurs. The maximum dose in our work was 1,000,000,000. Experience has proved that smaller doses are preferable to large ones with some patients; 5,000,000 to 100,000,000 may produce sufficient reaction for curative purposes and diminish the risk of a too great reaction. Absolute rest, much of the time in bed, with a copious fluid diet, chiefly milk, shortens the course of treatment, reduces the risk of chill with the reaction, and makes recovery more certain.

**SPECIFICITY OF VACCINE THERAPY.** The specific effect of autogenous colon-bacillus vaccine therapy is proved by the phenomena of reaction. This consists of the local reaction at the point of injection, which includes redness of the skin, tenderness, and swelling over an area from one to two inches square. This begins in one or two hours after the injection, reached the maximum in twelve to eighteen hours and gradually disappears by the end of forty-eight to seventy-two hours. A general reaction occurs in two to twelve hours, manifested by general malaise, aching of muscles, bones, and joints, more or less headache, more or less fever, sometimes preceded by a chill and leukocytosis. If the patient is up and about reaction is more severe—manifested by severe chill and fever. In many patients there is irritation manifested by pain, aching, etc., of the kidney, bladder, joint, group of muscles, etc., respectively, which is the seat of morbid change due to the colon infection. The specificity is further indicated by an increase in the opsonic index, and finally by an immunity manifested by the failure of reaction after vaccination and the disappearance of the bacteria from the urine. One should employ at the same time all rational measures to relieve the patient. General hygiene, personal cleanliness, correction of diarrhea or constipation, hematinics when necessary, and, as stated

above, surgical or mechanical measures to correct anatomical faults which interfere with proper drainage of the urinary tract.

Elsewhere in the paper I have stated that colon bacilluria is not an uncommon occurrence. In many individuals with this urinary infection there may be no perceptible effects from it. In other patients who suffer from some systemic infection, the conditions may be ascribed to the existing colon bacilluria without due regard for some other possible cause. This statement I think is necessary, because I have found that colon infection of the urine has been brought into the foreground by some physicians who have known of pathological effects due to it and who may misinterpret the condition and fail to look for or to find a real focal infection somewhere else in the body. We must not forget that focal infection of the tonsils, of the sinuses of the head, or of some other mucous tract of the body may produce systemic disease. Therefore, while I believe that colon bacillus infection of the urinary tract is sometimes a cause of not only local but also of systemic disease, I would caution those who find this infection of the urine not to be led astray by it, and to make sure of its relation to local or systemic evidence of disease by proof of its specificity by agglutinative, phagocytic, bacteriolytic, and other tests, and at the same time to look for other possible sources of infection before the treatment is begun.

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## PAROXYSMAL ARTERIOSPASM WITH HYPERTENSION IN THE GASTRIC CRISES OF TABES.

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AMONG the most interesting of the problems which the clinician has to solve is that of the interpretation of acute abdominal pain. The subject is a large one, and it is my purpose in this communication to deal with only one phase of it—that indicated by the title of this paper. The topic may best be approached by the presentation of a case which illustrates the main features of the condition under discussion.

Hattie T., aged forty-nine years, white, married woman, a cigar-maker, was admitted to Ward G, Johns Hopkins Hospital, October 9, 1909.

Her complaint was severe pain in the back and stomach, and headache. Her family history is negative. She has been married twenty-four years. She is the mother of six children, two of whom died in infancy. She had had several miscarriages, all occurring early in the pregnancies.



Except for vague "rheumatic" pains for some ten years she suffered from no disease until the present trouble began. About eight years ago she began to have attacks of pain in the back, indigestion, and pains in the joints, especially in the shoulders and knees. The pain in the small of the back was tolerably severe, and was sometimes associated with nausea. These attacks recurred at intervals. One and one-half years ago she separated from her husband, and since then the attacks have increased in number and severity. In May, 1909, the uterus, tubes, and ovaries were removed in one of the city hospitals, but since the operation she has been more nervous than before. She has suffered much from headache, frontal and vertical, and she thinks her eyesight has failed during the last few years.

The individual attacks begin with a feeling of a lump in the throat which cannot be swallowed (globus?). Vomiting soon comes on, so that nothing can be retained in her stomach, and she has extreme pain in the back and abdomen and complains of sensitiveness of the skin of the trunk. The pain is so severe that she usually weeps violently and tosses about in bed, grinding her teeth. She has never lost consciousness in an attack, nor has there been any disturbance of the sphincters. Her mind seems clear during the attacks. Her physician frequently was compelled to give her morphine for the pain. She has had more or less of the drug during the last five or six years. Since about a year ago there have been nearly two attacks per week, each lasting from a few hours to three days. She has noticed palpitation of the heart during some of the attacks.

On examination the patient was found to be somewhat emaciated; the skin was sallow, the muscles soft and flabby. There was no anemia. Her eyes were rather prominent; there was a tendency of the eyeball to run ahead of the lid in making von Graefe's test. The pupils were contracted, and reacted but little to light or accommodation, but it was thought on admission that this might be due to the morphine. There was no glandular enlargement. There was slight enlargement of the heart, the relative dullness extending to the left 10 cm. from the mid-sternal line. The radial and temporal arteries were tortuous and somewhat thickened. The lungs were negative, except for a moderate grade of emphysema. The stools contained some mucus, but no parasites or blood.

On the day after admission she began to suffer from severe pain in the abdomen and back, lying in a crouched position, crying constantly, and complaining bitterly. She vomited at short intervals. The vomitus was greenish in color and was accompanied by nausea. Chemical examination showed a total acidity of 42 per cent.; 23 per cent. of free hydrochloric acid; no lactic acid; no blood. Examination of the blood revealed: Red blood corpuscles, 4,258,000; white corpuscles, 13,800; hemoglobin, 92 per cent. Differential count: Polynuclears, 66 per cent.; large mononuclears, 7 per cent.; lymphocytes, 24 per cent.; and eosinophiles, 3 per cent.

An examination of the stool two days later revealed the presence of ova of *Trichocephalus dispar* and also ova of *Ascaris lumbricoides*.

On October 13 I observed her myself during a paroxysm of pain. The face was very anxious, the lips somewhat cyanotic, the eyes reddened and lacrymose. One got the impression at once that the pain was that of organic disease. The radial pulse was 124, regular but of very high tension, feeling like a fine whipcord under the finger. The blood pressure was measured at once and found to be about 190 mm. Hg. She was given an inhalation of amyl nitrite, and the pressure fell at once to 90. A short while after, however, the pressure again became high, going to 200 and later on to 210 mm. Hg. The knee-jerks were overactive; the plantar reflexes normal. The pupils did not respond to light. There was no tactile anesthesia of the chest, but definite analgesia in large areas in the lower extremities were present.

The urine contained no albumin or casts. Acetone was present, doubtless due to the prolonged vomiting, though the test for diacetic acid was negative. Palpation of the abdomen revealed nothing abnormal.

In spite of the active knee-kicks, I felt that the character of the pain and the vomiting, together with the sluggish pupils and the analgesia of the legs, made the diagnosis of gastric crises of tabes probable. This diagnosis received support also from the extreme hypertension due to arteriospasm accompanying the attack. I suggested that lumbar puncture be done and the spinal fluid examined. On the same day Dr. Kingsley withdrew 10 c c. of cerebrospinal fluid. It was under a pressure of from 150 to 200 mm.  $H_2O$ , clear and colorless. There were 50 cells per cubic millimeter, all lymphocytes. The fluid contained both globulin and serum albumin. These tests demonstrated the existence of either a luetic or a metaluetic lesion of the central nervous system.

Sensation was carefully tested on October 15, when the left lower extremity was found to be almost wholly analgesic and the right also, except for a portion on the lateral surface of the limb. There was also analgesia in the domain of the second thoracic of each arm. A patch of analgesia was found upon the right side of the scalp (Figs. 1 and 2). Touch was nowhere impaired and thermal sensation was not markedly involved.

On October 20 the eyes were thoroughly examined by Dr. Bordley. One of them had been dilated with atropine. The other showed extreme myosis and did not react to light and only imperfectly to accommodation. Stelwag's and von Graefe's signs were positive. Convergence was poor. There was advanced arteriosclerosis of the retinal vessels, some of the smaller arteries being almost completely obliterated. The veins were markedly indented by the arteries, and in places tortuous. There was no change in the papillæ nervi optici except hyperemia from obstruction to the venous circulation.

The Wassermann reaction done by Dr. Guthrie was found to be negative.

Examination of the urine: Normal in color; specific gravity, 1010 to 1018; acid; no sugar; no albumin. Microscopic examination was negative. Acetone was present only during the vomiting.

The course of the blood pressure is shown in the accompanying chart (Fig. 3).

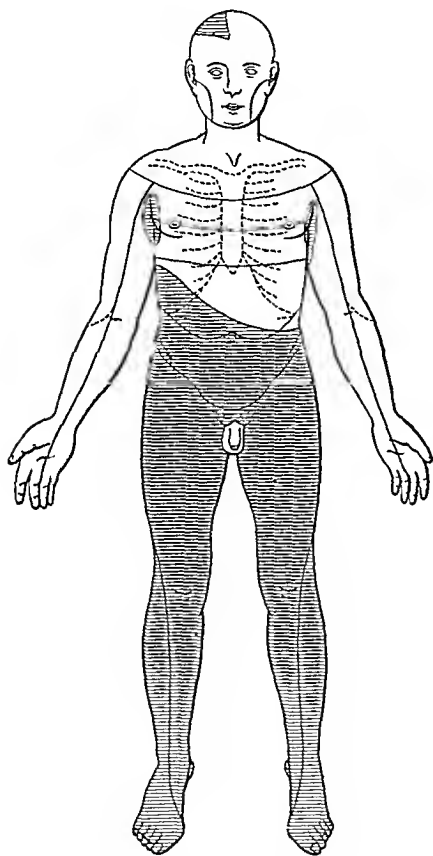


FIG. 1.—Analgesia at the first examination.

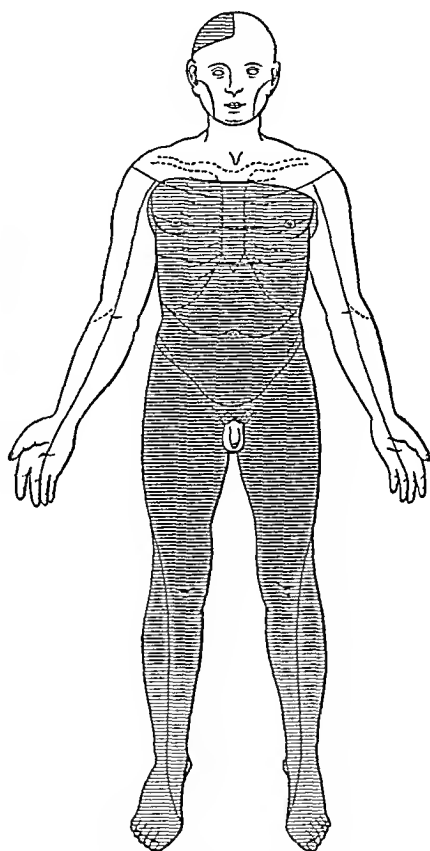


FIG. 2.—Analgesia at the second examination.

The patient's pain was relieved by morphine. As soon as the vomiting stopped she was given small quantities of milk every two hours. During the next five days she had only two attacks of nausea and vomiting. She began to have a good appetite and to feel very much better. The blood pressure (maximal) varied between 175 and 215 mm. Hg. until the 18th. On the 19th the maximal pressure was found to be only 120 mm. Hg., and since then it has varied between 110 and 125 mm. Hg.

Since the fundamental studies of Fournier upon the phenomena of early tabes the pains in the upper abdomen in this disease have

been classified under four main headings: (1) Crises in which there is vomiting alone; (2) crises in which there is pain alone; (3) the *grande crise gastrique*, in which the phenomena are complicated and violent, and include extreme pain, vomiting, and retching, with severe general symptoms; and (4) crises in which the appetite is entirely lost, though other signs may be absent.

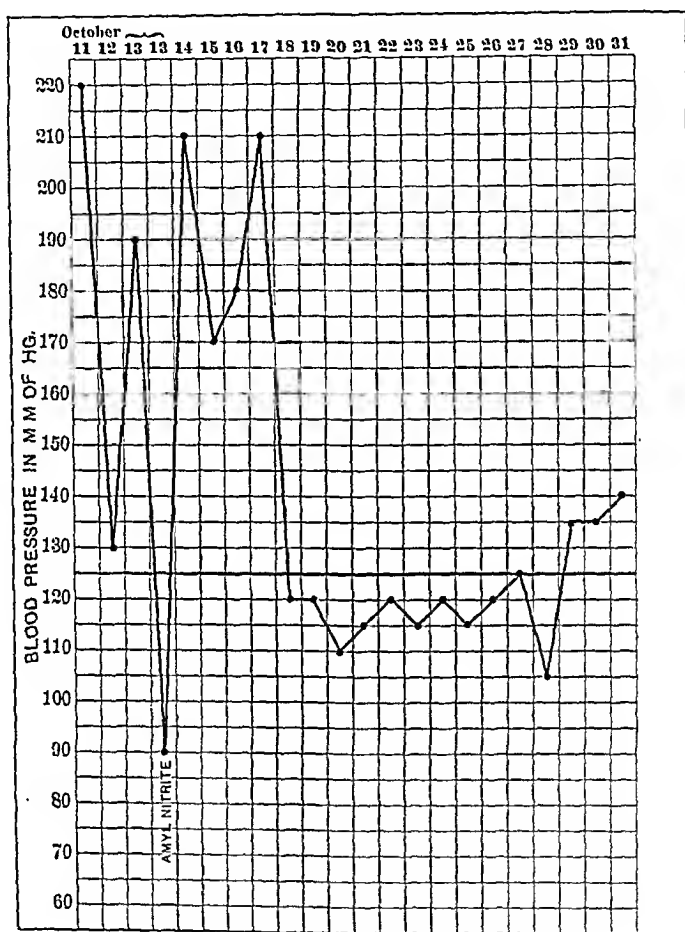


FIG. 3.—The course of the blood pressure.

The patient whose history has been given evidently suffered from crises of the third type, and it is to this form of gastric crises in tabes that I desire to refer, making it, however, distinctly understood that in the other three types of crises many of the features of Type 3 may be lacking.

In the crises from which this woman suffered the pain was situated in the upper abdomen and radiated into the back. The pain was accompanied by paroxysmal arteriospasm, with great elevation of the maximal arterial pressure. That the hypertension depended upon the arteriospasm was evident from the effect of amyl nitrite.

which reduced the maximal pressure promptly to 90 mm. Hg., though as soon as the effects of the nitrite had worn off the hypertension reappeared. The marked oscillations in the maximal pressure during the crises are evident in the blood pressure chart (Fig. 3). It was only after the pressure returned to normal and remained on the normal level that the symptoms disappeared. A study of similar cases in the literature indicates that partial falls of the pressure are significant only of remissions in the crises, not of termination. The abrupt terminal fall in pressure is striking, and the maintenance of a tolerably steady pressure at the low level after the period of hypertension seems to me most interesting.

There are at least three conditions in which attacks of severe abdominal pain with paroxysmal hypertension occur: (1) The gastric crises referred to above; (2) lead colic; and (3) the angina abdominis of arteriosclerosis. A number of cases of all three conditions have been collected and carefully analyzed by J. Pal.<sup>1</sup> In these cases, besides the pain and hypertension, the attacks presented several other characteristic features, including (1) constipation, (2) boat-shaped retraction of the abdomen, (3) in some cases meteorism, and (4) in many instances segmental sensory disturbances (usually hyperesthesia or hyperalgesia) in the root domains of the lower thoracic and upper lumbar spinal nerves.

There has been much dispute as to the origin of the pain in these cases and its relation to the hypertension. Some authors assume a primary neuralgic pain with secondary hypertension due to the pain; others, with Pal, regard the hypertension as the result of vasoconstriction of the small arteries of the stomach and intestines, and look upon the pain as due to stretching of nerves in the arterial sheaths of the same arteries proximal to their constricted portions, assuming that in these proximal regions of the gastro-intestinal arteries the arterial wall is distended and under very high pressure. The researches of experimental physiologists and surgeons tend to confirm the view that the only pain nerves in the stomach and intestines are those in the walls of the bloodvessels. It has long been known that the visceral peritoneum (not the parietal) is insensitive, and there is evidence to prove that even violent contusion of the intestine or stomach (such as crushing with Dupuytren's scissors) causes no pain.

In the gastric crises of tabes it is assumed that irritation in either the posterior roots of the spinal nerves or their continuations within the cord leads to a reflex vasomotor constriction which is most extreme in the splanchnic domain. If this explanation is correct we must assume that we have to deal in tabes at times with elective stimulation of posterior root fibers, for when tabetics suffer from lancinating pains in the lower extremities the blood pressure is

<sup>1</sup> Gefäßskrisen, Leipzig, 1905, pp. 1 to 275.

usually low and we must assume in such cases a reflex vasodilatation. In the gastric crises of tabes there is paroxysmal arteriospasm and hypertension, and we must assume here a reflex vasoconstriction. It is interesting that lancinating pains and gastric crises rarely occur together in tabes, though their alternation is not uncommon. This disparity in the symptomatology of incipient tabes, pointing to an elective stimulation of the posterior root fibers or their intramedullary continuations, has led me to think of our embryological knowledge of the posterior roots. Since the studies of Flechsig and, later, of Trepinski we have known that the fibers of the dorsal funiculi do not become medullated all at once. Definite groups of these fibers receive their myelin at very different periods, and Flechsig has subdivided the fibers into four distinct embryological systems.<sup>2</sup> The fibers of these different systems have different terminations in the cord and in all probability subserve different functions. It has also been shown, through the microscopic study of the spinal cord in cases of tabes, that a very distinct parallelism occurs between the areas degenerated in this disease and the embryological membership in the foetal cords. Furthermore, it has been shown that in tabes the sequence in which the several systems suffer may vary. It seems to me highly desirable, therefore, that cases of incipient tabes carefully studied clinically, which, through some intercurrent disease, come to autopsy before degeneration is advanced, should be most closely investigated microscopically. In this way we may hope for gradual enlightenment concerning the functions of the different systems of fibers contained within the dorsal roots of the spinal nerves.

The explanation of the phenomena other than the pain and hypertension in the gastric crises of tabes has also been attempted by various writers. Though the explanations thus far offered leave still much to be desired, opinion at present leans to the view that the vomiting is a reflex vagal phenomenon; that the constipation is due to paralysis of the intestine from ischemia due to the vasoconstriction; that the boat-shaped retraction of the abdomen is to be regarded as a reflex through the motor spinal nerves of the corresponding segments; and that the segmental hyperesthesia is to be thought of as due to "referred sensation" in the sense of Head, resulting from the violent impulses passing along the stretched perivascular sympathetic nerves and reaching the cell bodies (within the spinal ganglia) of the neurones of the lower thoracic and upper lumbar dorsal nerve-roots.

Since in arteriosclerosis attacks of angina abdominis closely resembling those of the grand gastric crises of tabes occur, it might be thought that the attacks in the patient reported above were due to the arteriosclerosis rather than to tabes, but, though the knee-

<sup>2</sup> L. F. Barker, *The Nervous System*, New York, 1899, p. 424 et seq.

kicks were lively, the pupils were very sluggish to light and, above all, the lymphocyte count in the cerebrospinal fluid was markedly increased, and the protein content of that fluid indicated the existence of a parasyphilitic disease. Moreover, vomiting appears to be less common in the angina abdominis of arteriosclerosis than in the gastric crises of tabes.

To one other point attention should be called, namely, the wide distribution of the analgesia and the great differences in this distribution at different periods. In the absence of disturbances of tactile and thermal sensation such an extensive analgesia could scarcely be due to the tabes. It seems much more probable that this analgesia and the globus of which the patient complained are hysterical manifestations complicating the more serious malady.

Should these severe crises continue in this patient, we shall consider the advisability of cutting intradurally the seventh, eighth, and ninth dorsal nerve roots on both sides of the body (Foerster's operation). In Küttner's case and in that reported by Bruns and Sauerbruch<sup>3</sup> the results were eminently satisfactory.

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## A STUDY OF FIVE HUNDRED AND FIFTY CASES OF TYPHOID FEVER IN CHILDREN.

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IN November, 1903, I read a paper before the Medical and Chirurgical Faculty of Maryland, the subject being a study of 337 cases of enteric fever in children. Now it is my intention to present a further study, by analyzing 213 additional cases, which have been treated during the half decade ended December, 1908.

In this study of 550 cases of typhoid fever treated in the Children's Hospital, District of Columbia, many obstacles, some insurmountable, were encountered. The period over which the investigation extends has been divided into three and a half decades, which seem to conform to the changes of ideas respecting this particular disease, embracing the years 1872 to 1908, inclusive. During the first decade all cases of typhomalarial fever were excluded, because this was then thought to be a distinct disease possessing only a few symptoms similar to those found in enteric fever. During the second decade these were included, because, by common consent, all typhomalarial cases were then recognized as enteric. In the

<sup>3</sup> Operativer Behandlung gastrischer Krisen. Foersterscher Operation, Mittheil. a. d. Grenzgeb. d. Med. u. Chir., 1909, xxi, 173 to 178.

third decade, cases of mixed infection which, in their clinical and pathological phenomena were identical with the typhomalarial diseases of the previous decades, have been incorporated. There might have been justification in swelling the number by including the many cases recorded in the first fifteen years under the headings *infantile remittent*, *remittent continued*, and *irregular* fevers, because I was then serving as an assistant physician in the hospital, and, in the light of our present knowledge, I now believe that such cases were genuine enteric fever. In spite of the fact that continuous connection with the hospital since 1876 has given me ample opportunities for careful study of those cases, I do not feel justified in changing the diagnosis made by my predecessors.

In the earlier years of practice, I was among the few who did not believe in the immunity of infants and young children to enteric fever. When some advanced the opinion (from which they have fortunately receded) that infants rarely, if ever, had enteric fever, and supported it by their failure to find the intestinal lesions of the disease in a large number of necropsies, I strenuously contended that infants and young children had a disease, which clinically was the analogue of enteric fever in the adult, and shortly thereafter presented to our local society the intestine from an infant showing lesions identical with those found in adults who had died of enteric fever. During the past ten years, I have seen an epidemic in one of our institutions, which spent its force upon infants under one year of age; and during the last five years have seen, in private practice, at least a dozen typical cases, several of which were used to illustrate a lecture on typhoid fever in infants, delivered at the Harvard Medical School in 1907. The clinical phenomena, including direct infection, were those of enteric fever, and I presented a specimen from one of the cases which showed ulceration and perforation of the ileum. Of late all doubts on this point have been dispelled by pediatricists generally. The acceptance of the theory of immunity unquestionably obscured the diagnosis in a number of cases, which might otherwise have added to the interest of this paper. Enteric fever in the child differs in degree only from that in the adult. While the clinical phenomena differ somewhat, the structural changes are identical, regardless of age.

There has been an annual increase in the number of cases treated in the hospital relative to the whole number of patients admitted. This has been about uniform, except in two instances, when it was much greater owing to the prevalence of enteric fever, in epidemic form, in the city.

SEASON. Of the 550 cases, 420 (76.54 per cent.) were admitted during July, August, September, and October.



TABLE SHOWING CASES ADMITTED BY MONTHS.

	Cases.		Cases.
January . . . . .	18	July . . . . .	78
February . . . . .	11	August . . . . .	153
March . . . . .	6	September . . . . .	119
April . . . . .	11	October . . . . .	70
May . . . . .	6	November . . . . .	38
June . . . . .	21	December . . . . .	18

SEX. Two hundred and ninety-six boys and 254 girls were treated, this being about the proportion in adults admitted to general hospitals.

AGE. At the organization of the hospital the maximum age of children admitted was fifteen years and the minimum two years. The maximum was gradually lowered until in 1888 it was fixed at twelve years, which accounts for the small number between twelve and fifteen years. There is a decided increase in the number admitted after the fourth year, which may be due to increased susceptibility at the beginning of school-life.

TABLE SHOWING AGES.

	Cases.		Cases.
One year . . . . .	1	Nine years . . . . .	61
Two years . . . . .	22	Ten years . . . . .	72
Three years . . . . .	29	Eleven years . . . . .	77
Four years . . . . .	27	Twelve years . . . . .	33
Five years . . . . .	50	Thirteen years . . . . .	3
Six years . . . . .	50	Fourteen years . . . . .	3
Seven years . . . . .	65	Fifteen years . . . . .	5
Eight years . . . . .	49	Not given . . . . .	2

MODE OF CONVEYANCE. It is a singular coincidence that the first case of enteric fever treated was attributed to the eating of oysters. This was in 1872, and yet it was quite twenty-five years thereafter that the oyster was recognized as a carrier of typhoid bacilli. Four cases were attributed to polluted milk, 25 to water, and 43 to contagion. In 478 cases no record was made as to the mode of conveyance. In the 43 cases attributed to contagion there was in every case evidence of direct exposure, in many instances several cases having occurred in the same family. The proof is positive in several cases in which water is mentioned as the medium. These cases came from a locality where enteric fever was epidemic at the time of their admission. The children, as well as many, if not all, of those affected, had drunk the water from a neighboring well, which, upon examination, was found to contain the colon and other bacilli, together with fecal matter.

MORBID ANATOMY. In 43 cases the necropsy revealed the characteristic lesions and in addition structural changes in the other organs. In 22 necropsies were not permitted.

*Perforation* was found in 17 cases, all being of the ileum. In 1 case three perforations were found, in 2 cases two, and in the remainder but one.

*Hemorrhage.* Twenty-eight deaths resulted from hemorrhage, but in no instance could the bleeding vessel be found.

*Spleen.* The spleen was almost invariably enlarged in the fatal cases.

*Liver.* No pathological condition was found in the liver. Abscess of the gall-bladder was found in one of the recent cases.

*Kidney.* Acute nephritis was present in 8 cases, the condition having been recognized before death.

*The respiratory organs* were affected in 7 cases, the *circulatory* in 3, the *brain* in 3, the *peritoneum* in 2, and the *bladder* in 1.

**MODE OF ONSET.** The disease was recorded as beginning insiduously in 361 cases, with diarrhoea in 17, malaise in 14, chills in 66, suddenly in 81, delirium in 7, cough in 5, vomiting in 8, headache in 6, synovitis, stupor, nausea, and tonsillitis in 2 each, and with coryza, adenitis, arthritis, erythema, sweats, and insomnia in 1 each; and the onset is not mentioned in 24 cases.

**SYMPTOMS.** *Temperature.* The course of the fever in children is usually of the remittent type, ranging from 103° F. to 105° F., and terminates by lysis. In this series the fever in 279 was remittent, in 24 intermittent, in 3 irregular, and in 2 atypical. The fever terminated by lysis in 241 and by crisis in 19. Posttyphoidal rise was noted in 4 cases and was due to some error in management. There were 11 septic cases that were most pronounced; 4 of these died. Recrudescence was noted in a very small proportion of cases. Chills were recorded in 73 cases, 13 being at the outset.

*Rose-spots* are not as frequent in children as in adults. They were present in 133 cases only, but, as about 20 per cent. of the cases were negroes, the percentage is not accurate. Sudamina and miliaria are more common in the negro child.

*Sweats.* More or less sweating at the height of the fever is not uncommon, and in this series it was so profuse in 10 cases as to classify them under the sudoral variety.

*Bed sores* so seldom occur in children that it was not regarded as important to consider them. Furunculosis occurred seven times.

*Circulatory System.* The changes presented by the blood differ slightly from those found in the adult. There was 1 case of pericarditis and endocarditis and one of endocarditis. One case of phlebitis of the femoral vein was noted.

*Digestive System.* Five cases of ulceration of the mouth, one being gangrenous, were recorded. One case of esophagismus of exceeding interest was found. The boy was seven years of age and had a typical, moderately severe, attack of enteric fever. At the height of the disease, in attempting to take drink or nourishment, a tonic spasm of the oesophagus would occur. This necessitated rectal feeding. After a long convalescence the patient recovered. Adenitis and parotitis occurred in 21 cases, most of which suppurated. Pharyngeal symptoms were recorded in 8 cases. Diar-

rhœa was of infrequent occurrence after the first stage, and when present was usually controlled by change of food. Hemorrhage occurred in 54 cases (9.8 per cent.); 27 (50 per cent.) of which died. In 1 case there were three profuse hemorrhages and the child recovered, while in the 27 fatal cases, but one hemorrhage was recorded. Meteorism and tympanites were noted in 14 cases. In 6 the distension was unusually great and caused intense suffering. Abdominal tenderness and gurgling were not as frequently observed as in the ordinary diarrhœa of children. Indeed, I regard the gurgling and tenderness in the right iliac fossa as of little practical clinical value. Of the 550 cases there were 17 (3 per cent.) with perforation, all of which were fatal. The diagnosis of perforation was made in every case within a few hours after its occurrence. In several cases an operation was proposed, but the parents would not permit it. In other cases peritonitis developed so rapidly that an operation was not deemed advisable. Three children were operated on when *in extremis*, and died a few hours thereafter. Enlargement of the spleen was recorded in 149 cases, but undoubtedly greater care in case-recording in the earlier decades would have increased the number. Epistaxis was found in 225 cases (40.9 per cent.), in many of which it was troublesome, and in 1 profuse and fatal.

*Pulmonary System.* *Bronchitis* was present in 31 cases in the earlier stages. *Pneumonia* was noted in 15 cases, one of which proved fatal.

*Nervous System.* *Delirium.* Children usually bear high temperatures much better than adults, but our statistics show a large percentage (56.18 per cent.) of nervous perturbations attributable to the pyrexia. The amount of fever formed no index of mental disturbances.

TABLE SHOWING TYPE OF THE DELIRIUM.

	Cases.
Mild . . . . .	51
Low, muttering . . . . .	155
Wild . . . . .	59
Maniacal . . . . .	8
Hysterical . . . . .	1
Stupor . . . . .	12
Coma . . . . .	1

The distinction drawn between *wild* and *maniacal* delirium is arbitrary. Those classed as wild were thoroughly unaccountable and required restraint; while the maniacal had hallucinations, delusions, and violent tendencies. *Convulsions:* In 16 cases convulsions appeared during the fastigium and not at the onset, as is the case in other infectious diseases in children. All of these cases were fatal. *Neuritis:* Local neuritis during convalescence was observed in 5 cases, all of which recovered. *Hemiplegia* with a fatal termination occurred once. *Post-typhoidal* insanity was

observed during convalescence in 9 cases, which had run a mild course without delirium. They were all due to faulty nutrition and promptly recovered with improvement in general health. I have reported 4 of these cases.<sup>1</sup>

*Ear.* Otitis media supervened in 15 cases (2.7 per cent.). Suppuration was profuse, but the disease only invaded the mastoid cells in 1 case. Deafness, sometimes profound, was frequently observed during the height of the disease, but always disappeared with the subsidence of the fever.

*Renal System.* Retention of urine is not often met with in children, but it was mentioned in 2 of these cases. The diazo reaction was applied in 182 cases, with 73 (40.1 per cent.) positive. [The test is made when the child is admitted, and daily thereafter, but the positive reaction is often delayed as late as the third week.] This test was abandoned several years ago. Albuminuria during the febrile stage occurred in 40 cases (7.2 per cent.), but usually disappeared during convalescence. Acute nephritis was noted in 15 cases (2.7 per cent.), 5 being fatal.

*Postenteric pyemia* infrequently manifests itself by abscesses. At one time there were 3 cases of perirectal abscess in the hospital. No case of multiple abscesses was recorded, but a boil on the head, buttocks, thigh, or back was not uncommon.

ASSOCIATION WITH OTHER DISEASES. In an institution in which tuberculous diseases prevail so extensively, it is somewhat surprising not to find acute miliary tuberculosis associated with, or directly following, an attack of enteric fever much earlier than 1909. Since then pulmonary tuberculosis has fatally attacked 5 convalescents, which are included in this series. Scarletina, measles, malaria, and pseudo-membranous pharyngitis and laryngitis also complicated the cases. Cancrum oris occurred in 4 cases, all being fatal.

VARIETIES OF FEVER. Typhoid fever in children presents such various modifications in its complex symptomatology that its classification as to degree depends entirely upon the observer. The course might be considered mild, and yet hemorrhage or perforation would cause an unexpected fatal termination; on the other hand, a case may be grave from the initial stage, and when least expected a rapid return to health may take place. It has been our custom to classify as follows:

	Cases.
Mild . . . . .	264
Moderately severe . . . . .	132
Severe . . . . .	142
Irregular . . . . .	2
Sudoral <sup>2</sup> . . . . .	10

<sup>1</sup> Trans. Amer. Pediatric Society, viii, 177.

<sup>2</sup> The term sudoral is used to define a condition in which there is profuse sweating during the fastigium.

RELAPSES. There were 48 relapses (8.7 per cent.), 4 cases having two each, with 1 death. In a case of septic enteric fever death occurred during the relapse. My experience has been that a relapse is of milder type and shorter duration than in the adult. The relapses here noted are true ones, but several spurious relapses have occurred which were of slight significance.

DIAGNOSIS. There have been but few mistakes in diagnosis, the greatest difficulty being to differentiate enteric from estivo-autumnal malarial fever, when the blood examination was negative. However, observation and repeated blood examinations finally settled the question. The Widal test was applied in 283 cases and gave positive results in 130 (49 per cent.) This percentage is a trifle lower than the results of other observers and may have been due to imperfect methods, which were unavoidable, before the establishment of a laboratory in the hospital. During the last five years a positive reaction has been obtained at some time during the course of most cases, but in most cases during convalescence, and in a few tests have been invariably been negative. No blood-cultures have been made.

MORTALITY. There were 65 deaths, a rate of 11.8 per cent. Taking the periods separately, we see the greatest reduction in the last decade and a half, which is unquestionably due to the methods of treatment employed. It must be stated that a number, especially colored children, died within forty-eight hours after admission, and, although they are included in the death-list, yet they might, with propriety, be excluded, which would reduce the mortality considerably.

	Cases.	Deaths.	Mortality. Per cent.
1872-1882 . . . . .	26	8	30.76
1882-1891 <sup>3</sup> . . . . .	59	12	20.33
1892-1903 <sup>4</sup> . . . . .	252	28	11.1
1903-1908 . . . . .	273	17	7.9

*Analysis of the fatal cases.* There were 32 boys and 33 girls, whose ages ranged as follows: Two years, 2; three years, 3; four years, 4; five years, 8; six years, 8; seven years, 8; eight years, 2; nine years, 6; ten years, 12; eleven years, 11; twelve years, 5; and fourteen years, 2. One was infected by oysters, 2 by milk, 5 by contagion, and 4 by water. The necropsy was made in 40 and revealed the characteristic local and parenchymatous lesions. In 4 subjects who had died of pulmonary tuberculosis, the intestinal lesions had healed. The onset was insidious in 40; by gastroenteric symptoms in 8; by angina in 1; by chills in 3, and suddenly in 11.

<sup>3</sup> It will be seen by the table that no cases are given in 1885. This omission, as well as that of 1897, was owing to the loss of records. In the annual report, 1885, 3 cases are reported, all of which recovered, which will reduce the mortality of the second decade to 19.35 per cent.

<sup>4</sup> In 1897 11 cases were treated and 1 died, which will reduce the mortality in the third decade to 9.27 per cent.

There were rose spots in 9. The fever was remittent in 38, intermittent in 6, atypical in 6, septic in 2, and not stated in 2. Epistaxis was noted in 32, chills in 16, intestinal hemorrhage in 26, perforation in 16, nephritis in 11, convulsions in 11, and pneumonia in 6. The delirium was wild in 28, muttering in 22, maniacal in 1. In 9 the spleen was enlarged. Such complications as bronchitis, pneumonia, peritonitis, cancrum oris, aphonia, gangrenous stomatitis, hemiplegia, pulmonary tuberculosis, mitral disease, and endocarditis, helped to swell the mortality. The variety of the fever was severe in 59, moderately severe in 5, and mild in 1. Thirty-five were treated by hydrotherapy; 3 by antiseptics; 6 by eliminative and antiseptic methods; 10 by antiperiodics; and 8 by antipyretics. Excessive diarrhœa was treated six times; hemorrhage fifteen; nervousness four, and cardiac weakness twenty-seven times.

**TREATMENT.** The general management of the cases was of the same character throughout, but the systematic methods of the trained nurse, which superseded the crude ones of the unskilled in the first decade, contributed much to the better results obtained in the second and third periods.

The *diet* which was uniformly liquid during the first three decades, consisted of milk and animal broths, except in 2 cases in which "pudding diet" was noted. I am not familiar with this last named food for enteric cases, nor was I able to ascertain its full meaning, but I suspect that the patients for whom the pudding was ordered were in the convalescent stage.

In the first decade there were twenty-six patients who were treated as follows:

	Cases.
Cold sponging . . . . .	5
Antiseptic treatment . . . . .	1
Antiperiodic treatment . . . . .	20

It will be seen that 20 received quinine. During this period Liebermeister's treatment was in vogue, and I can recall the large doses of quinine given, which had little effect upon the fever, but often irritated the stomach and increased the nervous symptoms.

In the second decade 59 patients received the following treatment:

	Cases.
Cold sponging . . . . .	23
Cold pack . . . . .	1
Antiseptic treatment . . . . .	5
Eliminative and antiseptic treatment . . . . .	4
Nervous symptoms treated . . . . .	32
Antiperiodic treatment . . . . .	30
Antipyretic treatment . . . . .	16

Daylight was beginning to dawn on the treatment, and the beneficial effects of reducing high temperature by external applications of cold were realized. This change of treatment was not well estab-

lished when that pernicious class of drugs, the so-called antipyretics, was introduced. Antipyrin was administered in 16 cases, 4 of which died. I remember with what pride we gave the synthetical preparations to demonstrate their power of quickly reducing high temperatures. It was quite two years before we realized that, while the temperature was being so beautifully lowered, the necessity for stimulation increased.

Quinine was now given to 50.8 per cent. of the cases and undoubtedly played its part in augmenting the number requiring stimulation.

In the third decade the 252 cases were treated as follows:

	Cases.
Hydrotherapy . . . . .	213
Antiseptic treatment . . . . .	33
Diarrhœa . . . . .	4
Hemorrhage . . . . .	1
Heart stimulants . . . . .	31
Nervous symptoms . . . . .	1
Antiperiodic treatment . . . . .	27
Antipyretics . . . . .	1

In this decade the treatment by the various *intestinal antiseptics* was introduced, but, after a fair trial, they were discontinued in my service, because I was not convinced that any benefit resulted from their administration.

Twenty-seven received quinine, because of mixed infection, but only 4 were given antipyretics; phenacetin was given to them to allay nervous manifestations and not to reduce temperature. Of 252 cases, 213 were treated by hydrotherapy. Under this head are included cold sponging, the cold pack, and tubbing after the method of Brand. The *regular* treatment recorded in the tables means one or all of the three methods, according to the indications in each case. About the same number as in the previous decade received stimulants, but for a different purpose. While in the second decade such drugs were necessitated by the cardiac depression from the coal-tar derivatives, now they were given as routine treatment in carrying out the Brand method.

In considering the results obtained in this one hospital during the last decade, it may not be wise to lay too much stress upon figures. The reduction in death-rate may not be due to the treatment, but by comparison with the mortality in preceding periods under different methods it emphasizes the following facts:

From 1892, the beginning of the third decade, to 1898, inclusive, the treatment followed was hydrotherapy, antiseptic, and antiperiodic. During this time 88 cases were treated, 10 of which died, giving a mortality of 11.36 per cent. At the beginning of 1899 the purely hydrotherapeutic treatment was begun and has been strictly followed throughout the remainder of the decade, with the result that of the 164 cases then treated 18 died, giving a death rate of 10.97 per cent.

Four cases of the last series died of pulmonary tuberculosis either during or directly following a typical course of enteric fever. We may rightly exclude them from our mortality list—when the death rate will be 8.54 per cent.

Some slight changes in treatment have been instituted during the last half decade. The diet was augmented in nutritive value by the addition of cereals, eggs, and bread to the prescribed routine of milk and broths. The patient's ability to digest such "soft food" was carefully watched and only two or three instances were recorded in which the semi-solid food had to be discontinued. I was rather skeptical at first as to the good results from giving semi-solid food to typhoid-fever patients, but I must confess to a conversion to the method so well portrayed by Shattuck. Realizing that diarrhœa is the exception in the child with typhoid fever, one can safely venture the use of liberal feeding. While an occasional case may not tolerate anything but liquid food, the majority will not only relish, but will digest and assimilate soft toast, cereals, and soft boiled eggs. By adopting this method, most of the heart-rending scenes of the sick-room will be avoided. The otherwise patient child no longer begs and cries for "something to eat;" there is no longer progressive emaciation until the little skeleton is covered by loose skin hanging in folds: relapses become less frequent; convalescence is shortened; and complete recovery replaces prolonged invalidism.

Our ideas on the Brand method have changed materially in that it was only used in three cases during this last period. Its beneficial effects have been demonstrated, but children do not require such heroic treatment; the sponge bath is quite as effective in reducing temperature, in allaying nervous perturbations, and in stimulating the activity of the emunctories. Intestinal irrigation was recently tried in a few cases, but its beneficial effect is not yet evident.

The table shows the methods of treatment:

	Cases.
Regular . . . . .	165
Brand . . . . .	3
Quinine . . . . .	22
Irrigation . . . . .	24
Antiseptic . . . . .	15
Eliminative. . . . .	3

In concluding, I desire to state that the cases were culled and the charts prepared from many imperfectly kept records, by the assiduous labors of Doctors Grasty, Turner, Riley and Smith in 1903, and by Doctors Ong, Titus, McLaughlin and Durney in 1909. To all of these I acknowledge my indebtedness.



**ARTERIAL HYPERTENSION.**

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ABNORMALLY high blood pressure, if once permanently established, is a condition of much significance, as it constitutes a grave departure from the physiological norm and entails certain structural and degenerative secondary effects in the arteries and heart of the most profound character. The mere fact of blood pressure being habitually raised above normal, even to a considerable extent above normal, does not seem necessarily to circumscribe the individual's activities, nor is it always accompanied by noteworthy subjective discomfort. The change to high levels is ordinarily a very gradual affair, the tissues progressively accustom themselves to the new standards of pressure, and the economy may not be disturbed. We consequently often find individuals with systolic readings over 200 mm. Hg. actively engaged in business and professional affairs, unconscious of any disturbance of health. Slowly but surely, nevertheless, the excessive mechanical strain to which their circulatory organs is subjected begets serious degenerative alterations, and finally if the process be not stayed the whole apparatus of the circulation will one day fall to pieces like the "Deacon's one hoss shay." Meanwhile no symptoms of alarming nature may arise until a sudden cardiac failure or an apoplexy tragically reveals the true state of affairs. Recently I was consulted by an active business man who for several weeks had unsuccessfully treated a cough, which was attended by asthmatic symptoms. He was found to have a blood pressure of 245 mm. with a pulse of 124, gallop rhythm, jugular pulse, pulmonary congestion, hepatic hyperemia, and albuminuria. In many a man above sixty we find a basic systolic murmur and accentuated aortic second sound indicating hypertension, or we may encounter indications of a relative mitral leak, with no complaint on the part of the patient beyond a certain puffiness on exertion.

Arterial hypertension, except when it occurs in association with chronic nephritis, is comparatively seldom met with before the age of forty. As an accompaniment of chronic nephritis it is often encountered in early life, even during childhood; otherwise it may be considered a disease of maturity. After forty years is passed the older the patient is when hypertension is diagnosed the more pronounced as a rule will be the element of arterial degeneration and the more apparent the cardiac secondaries. In early middle life unless the elevation of blood pressure is the result of nephritis it is apt to stand unique as the single physical indication of some obscure nutritive or toxic disturbance. In many instances of the kind hypertension

is the only thing present without or previous to the development of organic secondaries. Cook advocates the collection of these cases into a separate group for which he suggests the name "essential arterial hypertension." Under this designation he would include that residuum of cases in which after eliminating all the usual and known causes there remains no explanation for the one constant and only physical sign—hypertension of the pulse. In practically all of these cases, as he states, there is a certain element of cardiac hypertrophy, but it may be difficult to recognize. This definition very nearly coincides with the presclerosis of Huehard. I can best describe this type of case by clinical illustration: S. P., aged fifty years, was rejected at a life insurance examination for a policy of large amount, because he had a blood pressure of 165 mm. He consulted me to determine its cause. He was a perfectly healthy looking man of active habits and although a generous liver was not intemperate. He was an excessive smoker. Careful examination failed to reveal any indication of organic disease. His heart may have been hypertrophied, but regarding this, after repeated examinations, I still remained uncertain. The urine was free from albumin and casts and of normal quantity. He complained of flatulency, but was not constipated. His hygiene and diet were carefully regulated, his smoking moderated, and in a year the blood pressure had descended to an average of 135 mm.

This form of primary arterial hypertension is probably more frequent than we are aware, and if the sphygmomanometer were used on all men of middle age coming under observation, both in clinical routine and life insurance examination, attention would be directed to it oftener than is now the case. It is hardly likely that we have to do here with a different type of case from those we ordinarily class as arteriosclerosis with hypertension, or as chronic nephritis. We have encountered it in its incipency, that is all, before pronounced organic secondaries have developed to stamp the case as arterial, cardiac, or renal. Should the condition persist unmodified we would probably be able to watch the development of arterial fibrosis as the result of prolonged mechanical strain upon the vessels, of cardiac enlargement, casts and albumin, and all the flock of secondaries that characterizes the fully developed disease.

The relationship of arteriosclerosis to high blood pressure still remains difficult to define, notwithstanding the large amount of investigation and discussion devoted to the problem. It is a well known clinical fact that the most extreme degeneration of palpable arteries may exist without elevation of blood pressure above the normal (Dunin, Groedel, Elliott). Equally common in practical experience is the existence of a greatly elevated blood pressure with but slight fibrosis of accessible arteries. We have to account then for the circumstance of an individual with rigid calcareous radials presenting a normal pressure for his age, whereas another patient much younger and possessing vessels far less degenerated gives

pressure values double the normal. It would appear that hardening of the superficial vessels alone does not suffice seriously to disturb the normal circulatory pressure. It is necessary that we distinguish very positively between the clinical type of arteriosclerosis and hypertension. They do not by any means go hand in hand and when the two are found together they may only have an indirect relationship. The fact that in most cases of persistent high pressure some fibrosis of accessible arteries can be made out has probably led us to overestimate the importance of arteriosclerosis in elevating blood pressure. Undoubtedly stiff arteries may cause some increase in tension without the operation of any second factor, but that they can unaided produce the excessive values we deal with clinically is open to question. "Arteriosclerosis is an anatomical change, whereas high pressure is a functional disturbance." Instead of arterial changes giving rise to high pressure it is probable that as often as not when the two are found together the sclerosis has been produced by the long-continued strain on the arterial walls caused by the hypertension. As a rule, however, cases of hypertension do not live long enough to develop a high degree of arteriosclerosis. It is clear that some underlying factor not accessible to our present methods of examination must be responsible for the occurrence of high blood pressure in arteriosclerosis. This factor we may assume on general grounds to lie in some disturbance of the splanchnic circulation. In health a certain functional interchange or "give and take" exists between the systemic and splanchnic circuits, the systemic drawing upon the splanchnic at need and at other times using it as a storage for blood.

In disease this "normal balance" may be greatly disturbed and if the splanchnic vessels be the seat of sclerosis their reserve capacity will be reduced and the systemic arterial pressure in consequence raised and maintained above normal. This is practically the conclusion of Hasenfeld and Hirsch, who from clinical and pathological data contend that it is only when the vessels of the splanchnic area or the aorta above the diaphragm are diseased that high pressure develops in arteriosclerosis. For the present at least we may assume that when arterial pressure is persistently raised the terminal divisions of the vascular system (splanchnic and systemic) are principally involved in the sclerosis. This is of the highest practical importance for arteriosclerosis of the splanchnics and arterioles cannot be recognized by physical investigation during life, but may be inferred to exist with a fair degree of certainty from blood pressure observations. The prognosis in this type of case is very different and far graver than in that other order of sclerotics with stiff chalky arteries, but no tension. As Cook has emphasized, the outlook in the case of a robust looking man of fifty-five with a blood pressure of 200 mm., even with no appreciable arterial degeneration, is not so good as in the case of a man of sixty-five with rigid arteries and a pressure of 130 mm. We find many examples of the latter type in every old

peoples' home where they live on year after year eventually dying of an atrophy, cerebral or cardiac. The patient with hypertension is in daily danger of apoplexy or heart failure. The element of danger is the tension.

Fraenkel and Hasenfeld have pointed out that corpulent persons of a sedentary habit are prone to develop sclerosis of the splanchnic vessels with high blood pressure. There is much reason to believe that such cases are toxic in origin and it is probable that the chief source of the pressor toxins is the digestive organs. The argument of clinical experience lends weight to the contention of Russel that in non-nephritic cases the hypertension is caused by the presence in the blood of substances which are absorbed from the alimentary tract and are the product in one form or another of what has been swallowed as necessary food or as unnecessary indulgence. This does not imply that the big feeder must necessarily develop splanchnic sclerosis and the small feeder escape. The essential factor will prove to be the digestive and eliminative competency of the individual and the relative suitability of his diet. In summing up the relation between arteriosclerosis and high blood pressure we must acknowledge in the first place that the thickening of the vessel walls incident to age is capable of causing a gradual, but by no means extreme rise in the average arterial pressure. We see this in the slow increase of average pressure readings as life advances, a pressure of 140 mm. being accounted normal for a man of sixty-five years, whereas his son will have a pressure of 120 mm. and his grandson 100 mm. Should the pressure of such a man register persistently above 160 mm. and with this his heart show enlargement he may be regarded as having hypertension and we must invoke some cause other than his arteriosclerosis to explain it. Such a development means that in addition to a thickened artery he has a constricted one, the former an anatomical change, the latter a spastic condition produced by some toxic excitant circulating in the blood and causing hypertonic contraction of the arterioles, splanchnic or systemic (Russel).

It is hardly necessary to urge the importance of carefully investigating the condition of the urine in every instance of hypertension. The frequency with which chronic renal disease is associated with cardiovascular changes is well known and no factor is so potent as nephritis in the production of high blood pressure. If a diagnosis of chronic interstitial nephritis can be made it is not necessary to search farther for the cause of high pressure. At the same time it is to be remembered that greater care than ordinary is required to diagnose nephritis in the presence of arteriosclerosis with high blood pressure, owing to the fact that some degree of atrophy of the kidneys, manifested by slight albuminuria and casts, is almost always present as a consequence of those organs sharing in the general vascular deterioration. Moreover, almost all cases, no matter of what origin, showing blood pressures over 200 mm. will display some albumin in

the urine. It is unfortunate that no clear distinction is made in clinical literature between arteriosclerotic renal atrophy, and true contracting kidney. Every experienced clinician knows how vast the difference is in course, prognosis, and treatment between the two conditions, and yet it is only from experience and not from medical literature that one learns to appreciate the distinction. Chronic interstitial nephritis is an inveterate organic lesion showing severe toxic manifestations, a steady and even rapid downward progression, is not amenable to treatment, and has a bad prognosis. In every respect, no matter how similar may be its urinary and physical indications, arteriosclerotic renal atrophy is the opposite of this, being slow in development and progress as is the case with the sclerotic atrophies generally. A distinction between the two is important owing to the difference in prognosis.

Chronic interstitial nephritis gives rise to the highest systolic readings that are observed clinically, pressures of 300 mm. and higher being recorded. The highest record I have is 285 mm. in a young woman, who died a fortnight after in uremic coma. In a study of 60 cases of chronic nephritis<sup>1</sup> the average pressure was 190 mm. Chronic nephritis is essentially a disease of systemic scope, involving the heart and arteries as well as the kidneys. Arterial hypertension is one of its salient features. Notwithstanding occasional exceptions to the rule, high pressure is so significant that it constitutes one of the most valuable diagnostic indications of that disease. The use of the sphygmomanometer and the discovery of high pressure will at once put the observer on the alert.

The attempt to establish a working hypothesis to account for all the varieties of hypertension leads us face to face with the toxic theory. Arterial hypertension is best exemplified as it occurs in a group of chronic diseases having as their common essential characteristic, toxemia. In all probability the *materies morbi* consists of certain abnormal biochemical products present in the circulating blood. This is apparent in scarlatinal nephritis in which the tension rises a few hours after the appearance of albumin in the urine, entirely too early for the rise to be explained by the formation of arterial fibrosis. The high tension of uremia is another instance in point. For laboratory proofs we have the well-known fact that the pressor principle of adrenal and pituitary glands and also certain drugs (ergot, nicotin, digitalis) will raise blood pressure. That hypertension is a functional effect, as well as an organic product, we may infer from the clinical observation that measures designed to detoxicate the system (diet, sweats, cathartics) will result in some reduction of pressure in most cases of hypertension, and the therapeutic action of the nitrites could not be secured did the condition rest solely on a basis of structural change.

<sup>1</sup> Jour. Amer. Med. Assoc., April 13, 1907.

The end-effects of long continued high blood pressure are manifested principally in the heart and arteries. The arterial walls reacting to the excessive mechanical strain undergo a progressive structural deterioration to the great prejudice of their normal histology and vasomotor tonus. In the end vasomotor response may be so seriously disturbed that nitrites may fail to lower blood pressure. Peripheral resistance increases in this manner with the stage of the disease. A somewhat parallel sequence of events is apparent in the heart. At first in response to overwork the myocardium hypertrophies just as does the myarterium. The peripheral retard being persistent and increasing and the heart reserve limited, myocardial insufficiency becomes inevitable. The heart at first hypertrophies and then dilates in the face of continued overstrain.

The complications of arterial hypertension will be determined by the ability of the different organs to withstand the strain. On the part of the heart we observe hyposystole and asystole, of the arteries atheroma, of the kidneys albuminuria and uremia. A cerebral vessel may give way and apoplexy close the scene.

The symptomatology of arterial hypertension is general rather than special. There may be an entire lack of symptoms until vertigo or an attack of acute dyspnoea alarms the patient, or some cerebral accident occurs. The condition is often revealed quite unexpectedly during examination for life insurance. Frequently the earliest symptoms are of nervous type, irritability, depression of spirits, disturbed sleep, or it may be that the patient complains of bilious symptoms, flatulency, constipation, headaches, and vertigo. There is usually precordial discomfort and dyspnoea following effort and the patient rises once or more at night time to void urine. As a rule the night urine exceeds in quantity that passed during the day. A symptom noted in a number of my cases is a severe paroxysmal flatulency nocturnal in occurrence or developing on exertion. During the intervals between attacks there may be no complaint of flatulency, and examination at any time may fail to reveal special tympany or distention. Shortly after retiring for the night the patient may experience a feeling of distention and oppression across the lower chest or he may awake after a period of sound sleep with a feeling as if the stomach were full of gas. Instinctively he strives to relieve himself by gulping, drinking hot aromatic or alcoholic drinks, and the fact that comfort is reestablished, frequently after an hour or more, only when he has belched freely, confirms him in his idea that it is indigestion. The breathing is usually hurried, and palpitation may coincide. Attacks of this nature may develop after exertion, especially soon after meals and most frequently during the early part of the day. Bending over, lifting, straining at stool may precipitate the symptom. This development is probably similar in character and significance to cardiac asthma and denotes insufficiency of the right heart. All of the patients with this symptom whom I have seen,

have had enlarged livers and one a well marked jugular pulse. I have come to regard flatulency of irregular and paroxysmal occurrence in mature individuals as extremely significant, and I believe that every such case should be carefully investigated as to the cardiovascular condition. A typical instance of this character is the following case.

S. F., aged seventy-six years, and weighing one-hundred and ninety pounds, is a retired merchant of means, and boasts that he has never been sick in his life. He confesses that he has been a very hearty eater and heavy smoker, and has for years been constipated. Although rather spare in his limbs he is round-bellied and his face is ruddy and somewhat pigmented. He complains that for some months he has been greatly troubled with attacks of explosive belching of gas developing during exertion and interfering greatly with his activities. These attacks are frequent during the early part of the day, especially after breakfast and occur comparatively seldom and less severely toward evening. They come on during walking, especially if the weather is cold or it is windy or the walking rough. He is compelled to sit down or lean against a fence or building until he had relieved himself by belching. There is little intestinal flatus, and but slight dyspnoea between the attacks. He is somewhat puffy on exertion. He rises two to four times at night to void urine. He is found on examination to have a greatly enlarged heart, the apex 17 cm. from the midsternum; and a systolic blow at the mitral area reveals the leaf of dilatation. The blood pressure ranges from 190 mm. to 225 mm. There are no urinary indications of nephritis. This patient remained under observation for two months with slight benefit to his symptoms and then departed south to a more agreeable winter climate. Two weeks after his departure he died of acute heart failure.

It is noted frequently by patients with hypertension that smoking causes restlessness and cerebral discomfort and that heavy meals are not so well borne as formerly. Women are apt to complain of flushing and burning of the face, and if in the middle period of life are apt to ascribe it to the climacteric. I have noted as a prominent symptom in two cases pains of an anginoid character referred to the precordium, the left arm, or abdomen following exertion. Tachycardia and palpitation are complained of. As a sign of great significance and rather grave import, as it indicates the beginning of hypostole, is dyspnoea on lying down. The explanation of this development lies in the fact that the arterioles being contracted the blood collects unduly in the veins especially the splanchnic veins. When the patient is upright these veins act as a reservoir, but when he lies down the force of gravity tends to empty them into the right heart. This leads to overdistention of the pulmonary capillaries and dyspnoea. The only way rightly to interpret these symptoms is to take the blood pressure. With every individual of middle age com-

plaining of persistent functional disturbance this precaution should never be omitted.

Examination of the heart in cases of hypertension will reveal enlargement of that organ. This may sometimes be difficult of detection in fat individuals and in women with pendant breasts. In the earlier stages the heart sounds are usually clear, the first tone booming and prolonged, the aortic second loud, valvular, and ringing. If the ventricle has dilated the murmur of relative mitral insufficiency may be heard. Late in the case with the heart badly disorganized, the patient dropsical, and the pulse small and arrhythmic, it may become extremely difficult to determine whether the case is one of cardiac failure from prolonged hypertension or a valve lesion in the final stage of incompensation. The sphygmomanometer may afford us no help at this juncture, owing to the failure of the ventricle having so impaired the support of the circulation as to induce secondary low blood pressure. One must then fall back upon the history and the general features of the case to decide the point.

Analysis of the urine in arterial hypertension may reveal no morbid elements from the kidney, although in cases of some standing a few hyaline casts will usually be found. If chronic nephritis exists the usual urinary characteristics of that disease will appear to point to the origin of the hypertension. Renal permeability to albumin seems to be overcome when the blood pressure reaches or exceeds 200 mm., so that cases with very high pressures, whether primarily nephritis or not, usually have albumin in the urine.

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## THE USE AND ABUSE OF GASTRO-ENTEROSTOMY.<sup>1</sup>

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GASTRO-ENTEROSTOMY, "the keystone of gastric surgery," was first performed in 1881. Today this operation is being frequently made. The object of this paper is to excite discussion upon the bearing of the operation along the lines where it is proper as well as improper. The risks of gastro-enterostomy performed by an experienced surgeon are inconsiderable. The mortality of gastro-enterostomy in benign disease is low, 1 to 2.5 per cent. This is fortunate in a sense, and yet unfortunate if it encourages the performance of the operation in conditions in which it is not properly indicated.

A most important, essential, and interesting point is that metab-

<sup>1</sup> Read at a meeting of the Manhattan Medical Society, New York, December 17, 1909.



olism after gastro-enterostomy is not interfered with to the degree of making the operation objectionable on this account. It has been clearly demonstrated by observers, particularly Paterson, that metabolism is in no way seriously altered. It has been my experience, after observing a large number of cases several years after operation, that not only has the patient's digestive ability been in no way impaired, but that he was able to take more freely of food, even such as could not be digested before. The ultimate results of gastro-enterostomy have been most satisfactory. This has been demonstrated by collected cases, notably those of Mayo, Moynihan, myself, and others.

Formerly the most dreaded complication of gastro-enterostomy was regurgitant vomiting. This, since the no-loop operation has been done, is practically a thing of the past. I was unfortunate enough to see a few of these cases when I practised the long-loop operation, but have not had a case of the kind since doing the no-loop operation. One of my cases of regurgitant vomiting necessitated five operations before I was able to correct it. The cause of regurgitant vomiting was believed to be the presence of bile in the stomach from the afferent loop, but it has been established by experiments on dogs that bile in the stomach has no injurious effect on digestion or the general health. In confirmation of this, Moynihan has reported a case in which the result of rupture of the intestine at the junction of the duodenum and jejunum necessitated closing the duodenal end of the bowel and transplanting the jejunal end into the stomach, thereby causing all the bile to enter the stomach through the pylorus; the patient never suffered from vomiting, and remained in good health several weeks after the accident, until his death, which was caused by perforative peritonitis, due to the Murphy button. Some surgeons, notably Kehr, perform cholecystogastrostomy in preference to cholecystocolostomy.

It has been my practice to place an anchor suture one-half to one inch distant from the commencement of the efferent portion of the bowel, in this wise preventing angulation and consequent spur formation, thus minimizing the chances of obstruction to the onward passage of the contents of the afferent loop. I believe that the cause of regurgitant vomiting probably has been a mechanical defect at the site of the anastomotic opening, therefore faulty technique. Other complications after the operation, as detailed by Moynihan, are hemorrhage, internal hernia, separation of united viscera (leakage), formation of adhesions at or near the point of new opening, peptic ulcer, pneumonia, and diarrhoea.

I have never encountered hemorrhage. I have never had a case of internal hernia or separation of united viscera, or leakage. Internal hernia is prevented by careful suture of the margin of the opening in the mesocolon to the wall of the stomach. To my mind that is more rational than suture of the margin of the opening in the

mesocolon to the bowel. Suture of the mesocolon to the bowel, if followed by contraction of the marginal mesocolon, may so constrict the bowel as to cause obstruction of the anastomotic opening and interfere with the passage of the contents of the duodenum into the bowel beyond the anastomotic opening. In this connection I might say that the surgeon should be a good cutter and a good sewer to avoid mechanical complications. I have seen the formation of adhesions at or near the new opening; and also pneumonia; but never peptic ulcer or profuse diarrhoea.

The conditions for which the operation of gastro-enterostomy is indicated are: Chronic gastric and duodenal ulcer, with their sequels, perforation, recurrent hemorrhage, and cicatricial contraction; carcinoma of the pylorus, in connection with excision or alone by way of palliative treatment; benign pyloric obstruction resulting from stricture, adhesions, or angulation; gastric tetany; gastropsis, with loss of stomach motility, and therefore with stagnation and usually more or less dilatation; chronic dilatation, without gastropsis, with stagnation from loss of motility; infantile hypertrophic stenosis of the pylorus; duodenal cancer or tumor causing obstruction; duodenal fistula; the rare cases of plastic linitis of the stomach, in which the hypertrophy of the walls reduces the stomach to such a size that only liquid in small quantities may be taken and retained.

The conditions in which the operation is contra-indicated, therefore, in which the operation is an abuse, are: Acute dilatation of the stomach, gastric neuroses, dilatation without stagnation, advanced carcinoma of the pylorus, and gastric crises.

This operation does good in chronic gastric and duodenal ulcer by diminishing the acidity, by abating pylorospasm, and possibly by allowing the entrance of greater quantities of bile into the stomach, removing the condition which has prevented healing of the ulcer. About 80 per cent. of patients operated on for gastric ulcer by gastro-enterostomy recover. That gastric ulcer is frequently multiple must be acknowledged. It is true that we have no pathological evidence that gastric ulcer is healed following the operation of gastro-enterostomy, yet we have clear clinical evidence that this is so. The mortality of gastric ulcer treated medically is about 20 per cent., and at least 50 per cent. of cures, so-called, relapse, and probably not 25 per cent. of patients treated medically are really cured. The proportion of cases of relapse after cure following gastro-enterostomy is about 10 per cent.

If the ulcer is not located at the pylorus, the latter therefore opens, and the contents of the stomach will partly pass through it as well as the new opening. The churning and propulsive movements of the stomach, which are later taken up by the pylorus and carried on through the duodenum and small intestine, are not interfered with. Some of the stomach contents pass through the new opening, as the

cut circular muscular fibers, the agents in the propulsive movements, are attached to the margins of the new opening, and in contracting separate the margins of the opening and thus allow the stomach partly to empty through this route. In complete pyloric obstruction all of the gastric contents, as a matter of course, pass out by way of the anastomotic opening.

As this paper deals with gastro-enterostomy alone, I have said nothing about the excision of the gastric ulcer. There is a great difference of opinion as to the relative merits of excision and gastro-enterostomy. The strongest argument in favor of excision is the likelihood of carcinoma becoming engrafted on the ulcer scar. The decision, pro or con, is best made at the time of operation, according to the appearance and consistency of the ulcer. A thickened, greatly indurated ulcer is better excised, since it is impossible to determine whether malignant changes may not already have taken place, and experience tells us that a considerable percentage of those excessively hard and thickened ulcers do show carcinomatous changes. Unless there is a suspicion of malignancy, however, gastro-enterostomy is the operation of choice, as showing a considerably smaller mortality.

The operation is strongly indicated in cases of recurrent bleeding, in which the intervals between bleedings are growing shorter, and the amount of blood lost the equivalent or more than on previous occasions. The following case is an illustration of operation for this condition:

Miss —, aged twenty-six years. In 1903 she noticed the first symptoms, which subsequently suggested gastric ulcer. She was miserable for two years, when she was again attacked with symptoms referable to the stomach. In August, 1907, she had an attack of severe abdominal pain, continuing for three days. Nothing remained in her stomach; she suffered from nausea and vomiting, which continued for two weeks. On August 23, after taking a small quantity of beef juice, she had a very severe hemorrhage, followed by several smaller hemorrhages at intervals. I saw the patient on August 30, with the physician in charge, Dr. Branson. As she had not vomited for two or three days before my visit, and her condition was so wretched, we agreed to defer operation for a few days.

*Operation*, September 3, 1907. Exposure of the stomach showed a saddleback ulcer on the lesser curvature, four inches from the pylorus, with greatly indurated edges. Subtotal gastrectomy and gastro-enterostomy were done. Recovery was uneventful.

In hour-glass stomach gastrojejunostomy makes a part of the necessary interference. This operation alone will seldom suffice, as when made in the pyloric pouch only the obstruction to the passage of food from the cardiac pouch still exists, and when made in the cardiac pouch alone it will not drain the pyloric pouch; hence

it is necessary, in addition to gastro-enterostomy at the pyloric pouch, to do a gastrogastrostomy or gastropasty, so as to place the two pouches in communication.

Gastro-enterostomy is indicated when a perforated ulcer of the stomach or duodenum is sutured, if the patient is bearing the anesthetic well. It has always been my practice to do this operation in connection with the closure of the ulcer. I know there are many surgeons who take the opposite stand; nevertheless, I am of the opinion that it is proper to do it if the patients are operated on comparatively early. Patients that are operated on late after perforation die, do what one will. The additional time which gastro-enterostomy takes when closing a perforated ulcer of the duodenum or stomach is a matter of no moment if the operation is done at a timely season. The chief advantages of making the anastomosis is to make the patient permanently well after he recovers from the closure of the perforation, which is too frequently not the case when this is not done, the patient continuing to suffer from indigestion. In the event that another ulcer has been overlooked, this places the patient in the best position for permanent relief. The surgeon will have more confidence in closing the ulcer, particularly if it has indurated borders, and he will not fear having caused too much obstruction to the lumen of the viscus. The operation of gastro-enterostomy puts the part at rest and makes healing certain and quicker, and therefore lessens the risk of leakage; allows us to feed our patients earlier, which is of some moment in a certain percentage of cases. Yet I may say here that I never had any trouble in nourishing my patients for the first two or three days by the bowel, by giving saline solutions and expressed beef juice. In fact, I think patients, as a rule, do not require anything in the shape of food for two or three days after the operation.

In carcinoma involving the pyloric end of the stomach, too far advanced for radical operation, and the patient's general condition being fairly good, and indicating that, if able to take nourishment, his life would be prolonged for several months and his comfort increased, the operation is warrantable. I believe that gastro-enterostomy is often performed in carcinoma of the stomach that is radically inoperable, when it had better not be done, as it only adds misery to misery.

That gastro-enterostomy is the only alternative in benign pyloric obstruction due to cicatricial contraction, adhesions, or angulation goes without saying. The exception would be an occasional Finney operation in exudative contraction, yet I am of the opinion that gastro-enterostomy here is the better operation from the standpoint of ultimate results.

In gastropptosis with or without dilatation and with stagnation, and in dilatation with stagnation, gastro-enterostomy is strongly indicated, providing the patient has received treatment in the shape

of lavage, diet, gymnastics, and attention to general hygiene, without recovery. In dilatation, unless the case yields very quickly to diet and treatment, it should be explored. It is not fair to the patient to withhold relief in the presence of chronic dyspepsia that does not yield to medical means, thus exposing the patient to the greater risks of delay. The frequency with which chronic dyspepsia proves at operation to be due to some tangible cause is a striking fact in practice. The necessity for the habitual use of the stomach tube is sufficient indication for gastro-enterostomy.

In infantile hypertrophic stenosis, in which the symptoms persist in spite of lavage and careful feeding, gastro-enterostomy promises most, but must not be deferred until hope of cure is out of the question. In duodenal ulcer the rationale for gastro-enterostomy is the same as in gastric ulcer. In duodenal tumor, duodenal fistula, and gastric tetany, it may be necessary to resort to this operation. In plastic linitis I have seen excellent results. At present I have in mind one case of a doctor who had not been able to take anything but liquids, and these in small quantities, for a number of years, owing to this condition. Following gastro-enterostomy he was restored to practically a normal condition. The stomach in this patient was one and one-half inches in vertical diameter, two inches in fore and aft, with walls an inch thick.

The operation is abused if done in advanced cases of carcinoma with marked cachexia. I am quite sure that in many cases of carcinoma of the pylorus the operation is ill advised. The mortality of subtotal gastrectomy in the latter class of cases is so little greater than gastro-enterostomy, that I question the propriety of gastro-enterostomy in the presence of a growth that can be excised without injuring the pancreas, if the glandular involvement be not too extensive. Injury of the pancreas, if followed by escape of the pancreatic ferments, which cause necrosis of the tissues with which they come in contact, is a serious condition. When the profession awakes to the importance of opening the abdomen early in the case of chronic dyspeptics, gastro-enterostomy will have a small place in the surgery of carcinoma of the stomach, except in connection with excision. That the operation is much abused if done in cases of gastric crises we will all agree.

In acute dilatation of the stomach the operation of gastro-enterostomy will never be required if the stomach tube is used earlier and oftener in persistent nausea, not waiting until there is vomiting in that class of cases in which we are not surprised to see it. In my surgical work the stomach tube is used to the exclusion of any and all medication, formerly and still believed by many to be worth a trial. The time lost in giving medicines, with the hope that they will do good, is the very time that lavage is to be practised if we are to prevent this serious complication. In chronic dilatation, with or without prolapse, if there be no motor insufficiency or stagnation, the operation is useless.

There is no doubt that there are certain morbid gastric conditions which have been, and are still, classified as neuroses. What concerns us particularly is that set of gastric symptoms classed grossly as "nervous dyspepsia." Under this general term have been grouped the most diverse symptom-complexes, with, as a rule, but little understanding of the underlying principles of the case. It is true that there are certain disturbances in the gastric function, motor, secretory, and sensory, for which we can, by the minutest examination, find no organic basis. Besides grouping them into these three classes, we may also classify them as conditions of irritation or depression. Thus, gastralgia, nausea, and gastric hyperesthesia are prominent types of sensory disturbances; hyperchlorhydria and hypersecretion are well-known types of secretory disturbances; while atony, pylorospasm, and pyloric insufficiency represent well-known varieties of motor disturbance. Needless to say, motor, sensory, and secretory aberrations may all be combined in a given case, and it is by various combinations that the different types of so-called "nervous dyspepsia" are produced.

As a fundamental principle, we can safely state that a gastric neurosis without other neuroses or neurasthenic conditions is a most rare thing. The gastric symptoms, however, may so overshadow all others that attention is directed only to them.

In sensory disturbances we find more or less anorexia, or at least capriciousness of appetite, in almost every case. It is such a constant symptom that it is of little value; practically every sufferer from every form of gastric disease, real or imagined, complains of it at one time or another. True gastralgia I have found rarely. Of the secretory disturbances, hyperchlorhydria is the most important. Our ability to diagnosticate the condition by analyses of stomach contents and secretions is not great, yet extreme cases can be diagnosticated in this way, and do at times occur in the absence of anything that would seem to account for the condition. Atony of the stomach also cannot at times be considered as anything but a neurosis, and its treatment falls fully as much within the province of the surgeon as of the internist. In the diagnosis we are again confronted by the lack of exactness of methods of examination and the difficulty of fixing a standard with wide enough limitations to include all normal cases, and yet of sufficient definiteness to be a standard.

Finally, we have that vague group of symptoms, sensory, motor, and secretory combined, which, in the absence of any definite or tangible demarcation, has been called "nervous dyspepsia." It includes definite feelings of distress, pain or heaviness in the epigastric region, eructations, anorexia, gastric torpor rather than marked atony, intervals of excess of acid secretion, and an associated intestinal derangement, with almost invariable constipation.

The most important features in the diagnosis of any gastric

neurosis is the eliciting of a careful history, which will show the general neurasthenic condition of the patient. The presence of a manifest general nervous breakdown with an undoubted neurasthenia would at once predispose us to consider any gastric symptoms present as but local signs of a general process. Again, this run-down condition may be a secondary neurasthenia, due to a primary lesion which underlies both it, indirectly, and the primary condition of the stomach most directly. A patient with a latent but not symptomless gastric ulcer would soon show gastric symptoms, which might be considered nervous in origin, as well as a general neurasthenic condition, due to his sufferings.

Carcinoma in its early stages is much more often considered as a gastric catarrh or nervous dyspepsia than it is recognized. Anorexia, followed by the symptoms of a vague chronic gastritis or neurosis, when it occurs in a middle-aged person, is a condition which should excite our greatest apprehension, and be dismissed from consideration only after the most careful examination has been made—after the case, if obstinate, has come to operation.

Punctate ulceration of the stomach mucosa with small, early bleeding points may involve almost, if not quite, all of the gastric mucosa. In the absence of the classical signs of ulcer, which we often have in this condition, the hyperchlorhydria present has often been mistaken for the main lesion.

It has always been my opinion that in very many of the cases of vomiting regarded as primary neuroses we have really a symptom only of some lesion in or outside of the stomach which, for some reason or other, we have been unable to determine. Vomiting as a pure motor neurosis is regarded nowadays as far less frequent than it was thirty years ago, yet we occasionally see it.

The surgeon's principal duty as regards the true neuroses of the stomach is to recognize them, to separate them from secondary dyspeptic conditions due to lesions which perhaps it is within his province to treat. I regard the proposition to operate on these cases for the mental effect upon their general neurasthenic or hysterical condition as unsafe, illogical, and as setting a most dangerous precedent.

There is no exception, perhaps, to the general statement that gastric neuroses per se are not within the province of the surgeon. If we consider gastric atony and ptosis as really neuroses, when they are apparently primary, they form the exception. There are certain of these cases in which all medical and general treatment is unavailing, while a gastro-enterostomy promptly leads to recovery, by furnishing the stomach with drainage, which by its own force it is unable to secure. In ptosis I believe that gastro-enterostomy is the only logical procedure. This is true even in some instances in which the pylorus is entirely patulous. While I believe that an

occlusion of the pylorus is the main indication for gastro-enterostomy, I do not think it is the only one.

To make a gastro-enterostomy upon a patient with gastric neurosis pure and simple is nothing short of a catastrophe. Within the past year a patient came under my observation who had had several operations performed, the last of which was a gastro-enterostomy. The patient, a typical neurasthenic, as a matter of course was not only not benefited by the latter procedure, but made very much worse. After having her under my care for a number of days I determined to restore her stomach and intestines to a normal condition, minus the amount of bowel necessary for her to lose in order to cut out the portion involved in the anastomosis; this I did, with closure of the stomach, the patient being markedly benefited thereby for a time. I have recently learned that she is vomiting again and her condition is practically the same as before the first operation. There could be no better example of the futility of operation in gastric neuroses.

Being jealous of the benefits that surgery has conferred upon humanity, not the least of which are in this field, I do not wish to have discredit cast upon her efforts by operations performed upon improper indications. It is with some trepidation, however, that I advise against operation in gastric neuroses, simply because so many cases are thus incorrectly diagnosticated which would afford brilliant surgical cures. In giving this advice, therefore, it is with a plea for more careful observation to rule out any possibility of an organic lesion being accountable for the symptoms. We are justified in considering only those cases as neuroses which give a history clearly indicating other neurotic stigmas, with symptoms that vary greatly without apparent cause, or as the result of emotional states, and which give to careful observation no clue to an organic lesion. Better that such cases should come to exploration occasionally than to miss many true surgical cases. But I do not concur in the advice to operate upon these cases knowingly, nor, having unwittingly explored the stomach in such a case, to make a gastro-enterostomy or any other operation in the absence of a definite physical indication.

In conclusion, it is fitting for me to say that every surgeon should first be a physician. The surgeon should understand disease, its physical signs, and its differential diagnosis. The surgeon who does not possess this knowledge is not in a position to advise treatment. The surgeon should not be the mere human tool of the physician. I regret to say that surgeons are of two classes—the surgeon and the operator; the combination is what makes the true surgeon. It is to be regretted that the laity too often regard the surgeon as the last man to be called in. How often their distaste for the surgeon has been the cause of the fatality!



## HAVE WE MADE ANY PROGRESS IN THE TREATMENT OF GONORRHŒA?<sup>1</sup>

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So much has been said and written on the theme of gonorrhœa and its treatment that you may be disposed to ask why I should have chosen it for this evening's discussion. The answer to this question is, that for an indefinite time the impression has been growing into a conviction that we are getting better results than formerly in the treatment of gonorrhœa. Not that we are shortening the duration of an attack; for, although in some cases the disease can be promptly throttled, its duration still averages from four to six weeks; but (1) we are now able to mitigate the sufferings of the first or acute period, say of the first week. (2) We believe that there are fewer complications, and a diminished liability to them; as, for instance, to posterior urethritis with its liability to inflammation of the contiguous structures. (3) There is less tendency to become chronic and to the development of that formerly frequent sequel of gonorrhœa, stricture of the urethra. (4) It is now easier to insure the patient's attention to treatment, for there is a wider and better understanding of the danger of infection by latent gonorrhœa.

You will admit that anything relating to this disease continues to be of great importance; for apparently there is no lessening in the number of cases, but, on the contrary, a gradual and steady increase in their number. Dr. Victor C. Pedersen, who is in charge of the Hudson Street House of Relief on the west side of the city, tells me that there is a "normal" increase in the number of the cases of gonorrhœa. At this institution there are from 7800 to 8000 new patients per annum, and from 60 per cent. to 70 per cent. of these are cases of acute gonorrhœa. Dr. Swinburne, on duty at the Good Samaritan Hospital, on the east side of the city, informs me that in this hospital there are from 50 per cent. to 60 per cent. of new cases of acute gonorrhœa per annum. It is evident that as yet no propaganda of scientific instruction has reached this stratum of society, and, according to Morrow, Julianne, and others, the general morbidity in women, men, and children as a result of gonorrhœa is so great as to warrant the term *alarming*; and at all events it is sufficient to arouse within us the wish to do what we can to lessen the grave scourge.

Morrow says: "It is a conservative estimate that fully one-eighth of all human disease and suffering comes from this source. Moreover, the incidence of these diseases falls most heavily upon

<sup>1</sup> An address delivered at a meeting of the Society of the Alumni of Bellevue Hospital, New York, March 3, 1909.

the young during the most active and productive period of life. It is a fact worthy of consideration that every year in this country 770,000 males reach the age of early maturity; that is, they approach the danger zone of initial debauch. It may be affirmed that under existing conditions at least 60 per cent., or over 450,000, of these young men will some time during life become infected with venereal disease, if the experience of the past is to be expected as a criterion of the future. Twenty per cent. of these infections will occur before their twenty-first year, 50 per cent. before their twenty-fifth year, and more than 80 per cent. before they pass their thirtieth year. These 450,000 infections, be it understood, represent the venereal morbidity incident to the male product in a single year. Each succeeding group of males who pass the sixteenth year furnishes its quota of victims, so that the total morbidity from this constantly accumulative growth forms an immense aggregate. . . . There is abundant statistical evidence to show that 80 per cent. of the deaths from inflammatory diseases peculiar to women, 75 per cent. of all special surgical operations performed on women, and over 60 per cent. of all the work done by specialists in diseases of women are the result of specific infection. In addition, 50 per cent. or more of these infected women are rendered absolutely and irremediably sterile, and many are condemned to life-long invalidism. From 70 to 80 per cent. of the ophthalmia which blots out the eyes of babies, and 15 to 25 per cent. of all blindness is caused by the gonococcus infection."

On the other hand, Dr. E. A. Davis and Dr. Gehring<sup>2</sup> claim that the number of cases of ophthalmia neonatorum in the dispensaries is diminishing, because of better understanding of the care of the baby at birth.

Now the question naturally arises, are these impressions as to improvement in treatment shared by other observers? And will the opinions and teachings of others in the practice of genito-urinary surgery deepen or efface these impressions? Let us see what answer we shall get from authorities. I will quote freely from the literature of the subject.

1. What has been accomplished in relation to the duration of the disease? In my own practice, although admitting that the majority of cases last from four to six weeks, there are others (more in number than formerly), especially in the higher social strata, which terminate in two or three weeks. But there is an interesting unanimity of opinion on the part of authorities that the disease takes from four to six weeks to run its course in those cases, which do not become chronic.

For example, Watson and Cunningham<sup>3</sup> define "cure" as follows:

<sup>2</sup> Oral communication.

<sup>3</sup> Diseases and Surgery of the Genito-urinary System, 1909.

"By cure we mean not necessarily the cessation of the discharge, but its non-recurrence upon omitting the treatment and upon resuming an ordinary manner of living." They then say: "One frequently hears the claim that gonorrhœa can be cured within a week or ten days, or at least a fortnight. Personally we have no sense of shame in frankly confessing our inability to accomplish such results, *as a rule*, although we sometimes succeed in so doing. We consider ourselves and the patient fortunate if we obtain a cure at any time less than six weeks." R. W. Taylor<sup>4</sup> states: "In favorable cases a cure may be brought about in four to six weeks. Occasionally some patients get well in three or four weeks." White and Martin<sup>5</sup> state that the "prognosis, under favorable conditions, is good for recovery by the eighth week;" while Greene and Brooks,<sup>6</sup> without making a definite statement as to time, think that "it is better to postpone the active local treatment of urethritis until after the acute stage is passed and the discharge first becomes mucopurulent. This is generally about the fourth to the sixth week after the onset of the disease." Hyde and Montgomery are even less sanguine and consider that "usually a first attack, with favorable circumstances and good treatment, recovers in from five to eight weeks." Morton also states that "the percentage of recoveries in two or three weeks is small, and that the usual duration is six weeks." Finger and Casper, representative of the Germans, are unqualifiedly pessimistic, and while admitting that the disease ends in from five to six weeks, state that the prognosis is doubtful. On the other hand, Keyes, Senior and Junior<sup>7</sup> are decidedly optimistic, and quite positively state the duration to be "untreated, six weeks or more; but curable within two or three weeks by the irrigation method."

2. In regard to the mitigation of symptoms, although this amelioration may be inferred from such statements as "in from four to ten days all obvious discharge ceases," etc., I find very few definite statements; but as a result of my experience it may be confidently said that prompt treatment by one of the albuminoid preparations of silver (organic compounds), together with judicious hygienic measures resolutely carried out, will reduce the activity of the infection, proportionately subdue the inflammatory symptoms, and possibly modify the whole course of the attack.

3. In regard to the complications of gonorrhœa, we are met by contradictory statements and confusion of opinions. A study of systematic writers, in collaboration with Dr. Edward Preble, shows that the percentage of frequency of complications varies so much with individual experience that it is impossible to prove by the

<sup>4</sup> Genito-urinary and Venereal Diseases, 1900.

<sup>5</sup> Genito-urinary Diseases, 1907.

<sup>6</sup> Diseases of the Genito-urinary Organs and the Kidneys, 1908.

<sup>7</sup> Surgical Diseases of the Genito-urinary Organs, 1903, pp. 119 to 124.

evidence that complications were any more prevalent under old methods than at the present time. So far as blood infections and remote metastases are concerned, there are virtually no statistics given, while for epididymitis, cystitis, prostatitis, spermocystitis, etc., the figures show every variation. In Wossidlow's monograph (1903) the conclusions agree with those of other writers; namely, that acute posterior urethritis, according to the majority, is an all but universal sequel, while other writers find it much less frequent. Statistics of acute prostatitis vary from 3 to 70 per cent.; spermocystitis is said by some to be very rare, while others make it extremely common. There seem to be no figures for cystitis, as it is too readily confounded with posterior urethritis and prostatitis.

Uhle and McKinney<sup>8</sup> cite the combined statistics of Rollet, Tarnowsky, Jullien, and Finger—11,972 cases of gonorrhœa, with 2244 cases of epididymitis, or 18.7 per cent. The authors' own material represented 16 per cent. Neuberger<sup>9</sup> quotes Jordan, of Moscow, who compiled statistics which show that 30 per cent. of gonorrhœal patients suffer from epididymitis in hospital practice. In dispensaries and private practice the proportion, according to Jordan, varies from 7 to 17.3 per cent. The figures for dispensary patients are 11.7, but if the history of the cases was taken into account the proportion increased to 27.8 per cent. The joint testimony of several authors is to the effect that from 80 to 90 per cent. of gonorrhœal patients develop posterior urethritis. The author gives a series of 200 cases treated in the early period with protargol injections followed by Janet irrigations when the subacute stage was nearly over, with but six cases of epididymitis, or 3 per cent. Neisser does not use irrigations in the acute period, relying upon injections of the prolonged type. His proportion of epididymitis was 9 per cent. Tauska<sup>10</sup> gives an analysis of 17 statistics, making the percentage vary from 3.2 to 29.2 per cent., the average being 15 per cent. His material was 674 cases of gonorrhœa, 75, or 11.1 per cent., having epididymitis on admission, while 18 cases gave a history of the complication. The total of 93 cases was 13.8 per cent.

Lewin and Bohn<sup>11</sup> present a series of personal statistics on acute spermocystitis; the article also gives incidentally the relative frequency and relations of posterior urethritis, prostatitis, epididymitis, and spermocystitis. The authors have carefully studied 1000 cases of gonorrhœa from this point of view. Their figures appear to show that if posterior urethritis can be prevented these

<sup>8</sup> The Study of Two Hundred and Sixty-four Cases of Gonorrhœal Epididymitis, New York Medical Journal, 1907.

<sup>9</sup> The Prevention of Epididymitis and the Method of Treatment of Gonorrhœa in the Acute and Subacute Stages, Dermatol. Zeitschrift, 1907, xiv, 14.

<sup>10</sup> Pathology and Statistics of Epididymitis, Arch. f. Dermatol. u. Syph., 1908, 89, 255.

<sup>11</sup> Zeitschrift f. Urologie, 1909, iii, 1.

complications hardly occur; also that early recognition and prompt treatment of spermatoecystitis should often prevent epididymitis. Of the 1000 cases, 629 had posterior urethritis, that is, 63 per cent., and of this number the prostate alone was inflamed in 385 (61 per cent.); the seminal vesicles (one or both) in 38 (6 per cent.), and the prostate and vesicles together in 180 (29 per cent.). Added together, this makes 565 cases of prostatitis (about 90 per cent.) and 218 cases of spermatoecystitis (nearly 35 per cent.). Of the 218 cases of spermatoecystitis, 139 were bilateral, 79 unilateral, 47 on the left and 32 on the right side. In the 1000 cases of gonorrhoea were 124 recent cases of epididymitis (12.4 per cent.). With this number were 107 cases of prostatitis, 42 isolated and 65 associated with spermatoecystitis. There were 76 cases of spermatoecystitis, 65 associated with prostatitis, and 11 isolated. While the authors are not entirely clear on the matter, they give the impression that spermatoecystitis is responsible for many cases of subsequent epididymitis. Under the head of treatment, as already said, they agree that early recognition and treatment of it will prevent epididymitis. Of the 218 cases of spermatoecystitis, 156 were of the simple superficial or catarrhal type, 50 were examples of chronic inflammation with obliteration fibrosis, and 9 were instances of empyema. Three cases were not accounted for. Of the 371 cases of anterior urethritis alone, there were but 4 with complications, all cases of prostatitis. In this article there are two significant statements: (1) That if posterior urethritis can be prevented, complications hardly occur; and (2) that early recognition and treatment of spermatoecystitis will prevent epididymitis. These are in accord with and strengthen my first proposition.

4. Coming now to the question of treatment, it is interesting to note that the effort of most teachers is to simplify it, employing fewer remedies and a more expert procedure. The methods of thirty years ago show an uncertainty and complexity that does not exist today. Not only is therapeutics more effective, but pathology has been very much simplified. Since Neisser's discovery of the gonococcus we have had a definite means of diagnosis, and also a definite means of prognosis of the acute stage. Yet, as already said, no matter what be the form of treatment, the average duration of the acute stage of the disease remains from four to six weeks. Notwithstanding our better understanding of the pathology of the urethra and of the cause of the disease, nature still takes her own time to remedy the results of infection, and to restore to a normal condition, or as near normal as possible, the mucous membrane, which has been devastated. Whether the treatment has been expectant, or by irrigation, or by hand-injection, or by the combination of the expectant and any other method, it seems to take just about so long for a new mucous membrane to be formed. The inference is that our methods should be unirritating, and adapted to

the indications as the latter arise. In 1876 Mr. J. L. Milton, of London, compiled a list of 63 medicaments used for urethral injection, for some of which extraordinary virtues were claimed; such, for instance, as the cure of recent infections in from one to four days, with only two failures in 64 cases! But on the modern definiteness and simpler therapeutics Watson and Cunningham may be quoted. They say: "We do not propose to let ourselves stray from the narrow limits defined by the efficacious remedies which have earned a right to be seriously accepted as having an established value. Those which are worthy to be thus classed are the following: the silver preparations, protargol, argyrol, and nitrate of silver; permanganate of potash, and the astringent remedies, zinc and lead. The first three and permanganate of potash aim at the destruction of the gonococcus, or at inhibiting its activity to the degree that the urethral membrane shall have the power to repair sufficiently to repel its further attacks. The nitrate is of special value in the more chronic stage of the disease."

Notwithstanding the modern attempt at simplification, there is diversity of opinion as to method. In illustration I may make the following citations: Keyes and Keyes, Jr.,<sup>12</sup> say positively that in the previous edition Keyes, Sr., has not advocated irrigation, but that Dr. Chetwood's modification of Janet's method has given results never before obtained in thirty-five years of practice. The results are so much better that he recognizes their obvious superiority, giving Dr. Chetwood the whole credit.

R. W. Taylor<sup>13</sup> recommends zinc injections almost at the onset. Only in the declining stage does he recommend irrigation. In the very acute early stage, when the question of local treatment is a delicate one, he mentions weak permanganate and protargol as antiseptics, stating that they benefit but do not cure. He seems to imply that they may prevent posterior urethritis, but astringents and capsules are his main remedy. Under the paragraph entitled "Fads in the Treatment of Gonorrhœa" he scores the heroic use of antiseptics and ridicules the claims of rapid cure. There may be an apparent rapid improvement, but the discharge is not arrested and the mucosa become succulent, so much so that urination is hindered and bladder irritation develops. Patients seldom try this treatment a second time. He appears to discredit the apparent cures by Janet's method.

Marshall<sup>14</sup> advocates protargol followed by astringent injections as preferable to irrigations, which are irksome. He gives no local treatment if the parts are œdematous. The treatment of chronic urethritis is overdone, chiefly because of the introduction of the

<sup>12</sup> Surgical Diseases of the Genito-urinary Organs, 1903.

<sup>13</sup> Genito-urinary and Venereal Diseases.

<sup>14</sup> Syphilis and Gonorrhœa, 1904.

urethroscope. Patients expect this to be used in all cases, and it is often meddlesome. Instrumentation should be avoided except in very chronic cases.

Hyde and Montgomery (1900), unlike most writers, have a paragraph on prognosis. They regard local treatment as particularly suitable for the stage of decline. Pus is a contraindication. A theory that gonococci are to be killed is responsible for much permanent damage. Weak astringents, if any, should be used. It is best to reserve injections for a patient who has had complications, epididymitis, cystitis, etc.

Fuller<sup>15</sup> speaks well of the newer silver preparations; if used very early in the disease they may prove of much value. Argonin, as introduced by Jadassohn in 1895, he has used considerably. Protargol came out later. It gave good results in private practice where cases are seen early. Janet's method is given exhaustively, but the author believes it causes spermatocystitis, and hesitates to recommend it. He evidently prefers injections of the mild anti-septics when the case can be controlled. Astringents are never to be used until the declining stage, and then not over twice daily.

Morton<sup>16</sup> forbids the use of the astringents before the declining stage. Janet's method will check the purulent discharge in eight days in most cases, but spontaneous relapses occur even in the midst of treatment, and they are often repeated several times. A thin discharge for weeks may persist, so that ultimate recovery is not hastened. This method appears to prevent posterior prostatitis. It must be begun early to be effective. The expense, trouble, and inconvenience are against it, and the author does not appear to advocate Janet's method as a routine procedure; he probably prefers for this purpose the use of silver solutions as anti-septics. Treatment with protargol, 0.25 to 1 per cent., causes improvement in a few days; the acute symptoms subside directly. The protargol is now given in greater concentration, and after a few more days the discharge ceases; but if the protargol is stopped a relapse occurs. The percentage recovering in two or three weeks is small; in most cases five or six weeks are required.

Lydston,<sup>17</sup> in assailing specific and rapid cures for gonorrhœa, says that Janet's method should not be placed arbitrarily in this class. In practice it is very rare for a case to be treated rationally, because both patient and physician underrate the possibilities of the disease. Personal experience of cases is too often based upon simple, mild cases. Local injection is the most available treatment; irrigation requires time and money at best. Proper injections prevent strictures and complications. There is still a popular prejudice against injections; patients are wont to blame them for complications, and

<sup>15</sup> Diseases of the Genito-urinary System, 1900.

<sup>16</sup> Genito-urinary Diseases, 1902.

<sup>17</sup> Surgical Diseases of the Genito-urinary Tract, 1904.

some practitioners, by censuring the injection treatment, conspire with the prejudice. Lydston believes in the modern organic solutions of silver for their bactericidal action, preferring them to astringents, which may impair the defensive activity of the tissues. However, he combines ordinary antiseptics and astringents.

Baumann has a good chapter on prognosis. This in pure gonorrhoeal affections is favorable. In subacute and chronic forms it is conditional on several factors—duration, complications, treatment. No method of treatment is free from relapses. Complications are more frequent with chronic gonorrhœa. The author believes nitrate of silver to be the best local remedy. Germicides and antiseptics always irritate; the more antiseptic the more irritant. For irrigation he uses permanganate of potash, 1 to 2000 to 1 to 20,000, and this treatment is not contra-indicated even in the early stages—in fact, he finds it the most beneficial at this time. He also irrigates with nitrate of silver and zinc sulphate in weak concentration.

Greene and Brooks regard posterior urethritis as universally present. They use no local measures until the mucopurulent stage is reached. They object to astringents on theoretical grounds. Mild antiseptics will not injure outright, but are not recommended. Directions however, are given for those who wish to employ them. Then begins the treatment recommended by the authors; it is made to the posterior as well as to the anterior urethra, and irrigation with silver nitrate follows.

Von Zeissl,<sup>18</sup> like Finger, quotes Ricord's aphorism: "We know when the gonorrhœa begins; we know nothing as to when it will end." Many factors affect the prognosis in individual cases. Astley Cooper's dictum is fully borne out today: "In many cases, despite all remedies, the malady lasts so long that it is a reproach to our art." Under "treatment" he speaks of the difficulty of controlling private patients, pointing out that they are exposed to many prejudicial circumstances to which a hospital patient is not. Zeissl laments that the discovery of the gonococcus has not helped us in the treatment. Modern antiseptics, he says, give him no better results than do the older remedies. However, he washes out the anterior urethra with a soft catheter and a permanganate solution. He does this from the start, unless œdema and lymphangitis are present. Protargol may be substituted for the permanganate. He also recommends Janet's method as a later resource. He also uses ordinary injections at short intervals.

Finger seems to be decidedly pessimistic, and apparently does not believe that our methods show any superiority over former ones. On the other hand, he does not assert the contrary. He goes very thoroughly into the history of the treatment, and finds that many of

<sup>18</sup> Frisch and Zuckerkandl's *Handb. der Urologie*, 1906, 111.



our modern resources are not really new. He finds syringes two hundred years ago differing in no wise from those of today. He also describes the great activity of the specialists of a generation ago in regard to the problem of treatment. He believes in weak protargol injections from the onset, unless œdematous swelling, bloody pus, and phymosis or paraphymosis are present. But as to the uncertain cure and its complications he seems to believe that the disease is the same old unknown quantity it was at the dawn of scientific medicine.

Wassidlow writes in a less pessimistic vein than Finger, but nowhere does he state or imply that our knowledge has progressed in recent years. Neither is the contrary statement made or implied. In a new edition of his book, Casper seems to be as pessimistic as Finger. Under "prognosis" he states that it is doubtful if the majority of cases do not become chronic; while in the chronic stage excesses of any kind may set up acute exacerbations, with all the attending dangers of complications.

Quite a number of writers, however, record their belief that we get better results than formerly. Janet, in his latest article (1907), appears to take a somewhat similar view. On the other hand, all of these continental experts who have been authorities for many years, dating back to pre-irrigation days, do not commit themselves.

In a very interesting article, Streiff<sup>19</sup> shows that irrigation is by no means a new resource. Morgan, of Dublin, employed it in 1869; Durham (Guy's Hospital) in 1870; Windsor, of Manchester, England, in 1871, using permanganate 1 to 1000; Reginald Harrison in 1880; Holbrook Curtis in 1883; Halstead and Van der Poel in 1886; Brewer in 1887, and Reverdin in 1892; all of them preceding Janet; and even earlier than they was Serra, who used irrigation of plain water in 1831. All of these pioneers irrigated the penile urethra alone. Another series of men irrigated the bladder and incidentally the posterior urethra: Cloquer (date not given), Diday in 1839, Reliquei in 1871, Bertholle in 1877, and others. Janet, however, originated modern urethrovesical irrigation, and also the theory that it cured by producing serous reaction and preventing the deep proliferation of gonococci. The author regards Janet's method as a logical development of bacteriology and antisepsis.

Janet's technique has been modified in various ways, and a great number of substances have been substituted for permanganate. In France nearly all surgeons and specialists use the irrigation in some form. They wait for the subsidence of the inflammatory phenomena. Irrigation has some enemies who do not believe in exposing the bladder to possible infection, and who rely upon injections and balsamics.

Streiff says nothing whatever as to the superiority of modern

<sup>19</sup> Old and New Treatment of Urethritis, Thèse de Paris, 1908.

measures. A century ago, or thereabouts, balsamics had superseded local treatment. The latter returned into vogue, but not until the discovery of the gonococcus and antiseptics did it receive its modern endorsement. Streiff claims that the modern treatment of urethritis, including lavage, instillation, use of the endoscope, ointments, sounds, massage, etc., is entirely surgical in its tendency.

My own recollection of what may be termed the era of irrigations in its different stages is still vivid. There was also an era of nozzles for insertion into the meatus urinarius. Many were the zealous experimenters. Everybody devised or modified a nozzle; and every nozzle was provided with both an inlet and an outlet tube, in order to regulate within the urethra the exact pressure of the irrigating fluid. We also "felt our way" with the strength of the germicide, in order to obtain an unirritating and yet efficient solution. At that epoch the bichloride of mercury was an efficient germicide when applied in proper solution to external wounds; would it not be equally efficient in gonorrhœal infection? Acting on this theory, I made an experiment at the City Hospital. I irrigated a considerable number of cases with bichloride of mercury, the solutions beginning with a strength of 1 to 6000. Any one who knows the irritating effect of that solution can imagine the warmth of the reception I received from the patients when I made my next visit to the hospital. The same experimentation was taking place at the Vanderbilt clinic and at the Outdoor Department of Roosevelt Hospital. The result of our combined experience and of our patients' tribulations was to reduce the solution to its proper strength, 1 to 20,000 or 1 to 30,000. Other substances, such as boric acid, hydrastis, methylene blue, and permanganate of potassium were also experimented with.

The house surgeons to a man were enthusiastic over the irrigation treatment, and were eager to employ it in each and every case. When they asked me what antiseptics they should use, I said, "Whichever you please." And now happened a curious thing, to wit, that their choice seemed to be determined in every case by the complexions of the house surgeons. I will not say *post, ergo propter*, but, as a matter of fact, all the blond men chose to experiment with plain white solutions or with methylene blue, while the brunette men invariably treated their suffering patients with the red permanganate of potassium. I leave the explanation of this to the metaphysicians.

My own conclusions in regard to the irrigation method were that it did not readily control the symptoms, but, on the contrary, that it was even liable to aggravate them. In many cases of acute gonorrhœa the patients can hardly tolerate their own urine passing through the urethra; therefore the introduction from without of a fluid which, even with the most watchful care, may overdilate the canal, is liable to cause traumatism and aggravate the conditions. Fur-

thermore, as time went on I became convinced that these irrigations not only did not shorten nor mitigate the attack, but that posterior urethritis was more prevalent, and that therefore inflammation of the contiguous structures, the prostate, the epididymis, etc., was likelier to occur. Moreover, the irrigations were inconvenient, they were sloppy, and because of the time required were difficult to carry out. Consequently, for acute gonorrhœa a change was made from that method to the one I now prefer. In chronic states irrigations may have their place; but even then only in exceptional cases.

There is a method called by the Germans the "provocative method." Zieler,<sup>20</sup> chief of Neisser's clinic at Breslau, who evidently represents the opinion of many of his colleagues, believes that whatever cures gonorrhœa can do so only by exciting hyperemia and serous transudation. The "inflammatory serum," as he terms it, is fatal to the deep proliferation of gonococci, which tend to return to the surface, where also many have been present from the beginning. In these more exposed situations they may be destroyed by antiseptics. The benefits of irrigation he attributes solely to the hyperemia set up mechanically, not at all to the permanganates. Protargol, argyrol, etc., are both hyperemizing and antiseptic, hence the good results from their use. The old-fashioned astringents are contra-indicated because they antagonize the hyperemic tendency and permit the deep proliferation of gonococci.

German physicians use the expression "provocative treatment" for the use of mechanical or chemical irritants intended to cause hyperemia, transudation, and destruction of gonococci. A writer having termed Dr. Carl Alexander's (Breslau) hydrogen peroxide treatment a "provocative" measure, the latter replies,<sup>21</sup> stating that his (1 per cent.) injection or irrigation does not belong under this head. He uses it to oxidize and destroy the gonotoxin. Further, the liberation of gas in the urethra exerts a mechanical action on foreign material, but not an irritating one. He regards his procedure as an addition to our resources; if it fails now and then, so do all methods. My own experience with hydrogen peroxide was not at all satisfactory; though it was not used by irrigation, which I agree with Kreissl<sup>22</sup> is a step backward, and gives poor results, tending to complications and chronicity. With the advent of the albuminoid salts of silver, we have had at our disposal better means of controlling the infection. Especially if used in the early stages of the disease, they will, in a large proportion of the cases, modify its progress and lessen the liability to complications. Their use by the hand-injection method, followed by such other means as may be indicated in the later stages of the malady, will meet all the requirements. The salts of silver are well under control; they

<sup>20</sup> Münch. med. Woch., 1907, 305.

<sup>21</sup> Zeitschrift f. Urologie, 1909, iii, 1.

<sup>22</sup> Urogenital Therapeutics, Chicago, 1908.

can be used in the most intolerant urethra without aggravating the patient's condition, and they can be placed in the hands of the patient himself. But it must not be overlooked that the latter must also be *treated*. Doubtless you will think it a mere truism to say that a patient's habits, social condition, etc., affect his vital processes. But we must take advantage of whatever physiology can do to limit the supply of pabulum to the infection and assist in strengthening the resistance of the tissue, and therefore it is as important to consider the patient's environment as to give him local treatment.

To me a very important fact is that the human urethra is now looked upon with what might be termed greater respect. This is not merely a speculative statement. It has a practical application. The old-time, coarser point of view, that the urethra was a mere "water pipe," and that if an individual subjected himself to conditions which infected this conduit he was the victim of his own folly, and, to use the common phrase, "it served him right." This view naturally tended to coarse and unsympathetic treatment. But it is now recognized that the urethra is a delicate, highly endowed organ, susceptible to grave local damage, and that its infection may be propagated to distant, even to vital organs, and to innocent persons. Based upon this, together with a knowledge of the specific cause of the disease our methods have become more definite, and our technique more delicate and gentle. Therefore there is ground for the statement that the average case shows less tendency to become chronic; and with our ability to inhibit the activity of the infection when the case is seen early there is less likely to be a posterior urethritis and, therefore, less liability to infection of the contiguous structures.

The subject is a large one, and much remains to be accomplished, yet, notwithstanding the dubious tone of the literature which I have tried to review I am satisfied that real progress has been made in the treatment of gonorrhoea.

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## HELMINTHIASIS IN CHILDREN.

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THE study which it is the object of this paper to record was undertaken in the effort to determine: (1) The frequency with which children between the ages of two and twelve years harbor intestinal worms; (2) the species of parasites harbored and the relative frequency of their occurrence; (3) the number of cases in which the common

intestinal worms are responsible for symptoms, and the nature of the symptoms produced; and (4) the occurrence and significance of eosinophilia in infections with intestinal worms. These investigations were based on the discovery of intestinal worms, their parts, or their ova in the feces. Whenever possible, the parasite was obtained after treatment, and in positive cases the blood was examined to determine the percentage of hemoglobin and the percentage of the eosinophile cells. The technique used in making the examinations will be given in some detail under the general discussion of diagnosis.

In this paper it is only intended to discuss the results of these investigations and to consider phases of the subject of helminthology which have a practical medical bearing. No attempt has been made to review the enormous literature, but work will only be cited which has a bearing on the investigations or is not to be found in the usual text-books. The investigations were conducted upon 310 children between two and twelve years of age. For purposes of convenience and accuracy the cases have been divided into two groups. The first group comprises 30 cases, the second 280.

The first group of thirty examinations were made entirely on the basis of suspicious symptoms, and were in no way consecutive; hence they are of little statistical value. This portion of the work extended over a period of four months, and the children examined suffered from obscure nervous or gastro-intestinal disorders, which were not explained by the history or physical examination. This group also includes 4 cases in which the parasites had been seen previous to admission.

As shown in Table I, twelve of the children in this group harbored intestinal worms, and, with the exception of one case (VII), the relationship of the symptoms to the presence of the parasite is shown by the influence of treatment. In the case mentioned the child disappeared from observation before treatment could be instituted, and in consideration of the fact that the parasite harbored rarely produces symptoms, this case must be considered doubtful. Three other cases (IV, V, and XII) were lost track of after treatment was begun, but the nature of the symptoms and the improvement with treatment give sufficient indication that the intestinal worms were the causative agency. The parasites found in the 12 positive cases were as follows: *Ascaris lumbricoides* in 2 cases, *Trichuris trichiura* in 2 cases, and *Oxyuris vermicularis* in the remaining 8 cases. The symptomatology and blood examinations will be dealt with under the headings of the different parasites.

The second group comprises 280 examinations, which were made as nearly consecutive as possible, on all children within the prescribed age limits from families whose members were under treatment at the clinics. These investigations extended over a period of thirteen months. From this group of 280 children, 80 (28.57

TABLE I.—POSITIVE CASES FROM 30 EXAMINATIONS MADE ON PATIENTS WITH SUSPICIOUS SYMPTOMS.

No.	Sex and age.	Nationality.	Parasites.	Symptoms.	Blood Examination.						Result.
					Polynuclear cells. Per cent.	Lymphocytes. Per cent.	Large mononuclear cells. Per cent.	Eosinophiles. Per cent.	Basophiles. Per cent.	Hemoglobin. Per cent.	
1	Male 3½	U. S.	Ascaris lum- bricoides	Fever. Temperature, 101° to 102° F. at night for ten days. Very restless during sleep, frequently cried out as if in pain. Frequent vomiting. Loss of appetite. Constipation. Sudden onset of illness.	36.0	40.0	10.1	12.1	0.2	70.0	Recovery after expulsion of worm.
2	Male 3½	Parents German. U. S.	Ascaris lum- bricoides	Ill three months. Irritable, loss of appetite, poor color, loss of weight. Jaundice one week. Passed roundworm four months ago.	40.8	30.3	16.1	12.6	0.8	65.0	Improvement after expulsion of two worms.
3	Male 4	Father German. Mother U. S.	Oxyuris ver- micularis	Loss of weight. Attacks of pain in lower portion of abdomen. Genital and nasal pruritis. Restless at night. Appetite poor. Worms seen by mother.	40.0	39.1	13.2	7.0	0.6	75.0	Improvement with treatment. Recovery in one month.
4	Female 5	U. S.	Oxyuris ver- micularis	Rectal irritation at night. Sleep interrupted. Irritable. Poor appetite. Constipation. Worms seen by mother.	58.1	18.2	13.0	8.0	1.0	—	Improvement for one week. Lost track of.
5	Female 6	U. S.	Oxyuris ver- micularis	Genital pruritis. Masturbation. Vulvitis. Loss of appetite, slight loss of weight. Mother not aware of infection.	53.2	25.0	18.3	2.1	0.5	60.0	Improvement for ten days. Disappeared from observation.
6	Female 7	Russia	Oxyuris ver- micularis	Nasal and genital pruritis. Loss of appetite, loss of weight. Mother not aware of infection.	60.0	21.2	14.0	3.3	0.1	60.0	Recovery with treatment.
7	Male 7	U. S.	Trichuris trichiura	Loss of weight, anemia, loss of appetite.	40.0	30.3	24.0	4.0	1.2	55.0	Lost track of. Treatment not given.
8	Female 7	U. S.	Oxyuris ver- micularis	Loss of weight and appetite. Sleeplessness, night cries. Nasal pruritis. Had passed round worm. Mother not aware of threadworm infection.	52.2	24.0	10.0	12.6	0.4	—	Improvement with treatment. Complete recovery in five weeks.
9	Male 7	U. S.	Trichuris trichiura	Anemia, loss of weight. Puffiness of lower eyelids. Appetite, sleep, and bowels normal.	Red blood cells, 3,100,000 per c.mm. White blood cells, 6000 per c.mm. Nucleated red cells (normoblasts) 43.6 40.0 16.0 0.3 — 40.0 40.3 35.0 18.3 6.0 0.1 75.0						Gradual improvement with treatment. Hemoglobin, 65 per cent. at end of eight weeks.
10	Female 8	U. S.	Oxyuris ver- micularis	Restless at night. Rectal irritation. Appetite normal. Worms seen by mother.							Recovery.
11	Female 8	U. S.	Oxyuris ver- micularis	Headache, sleeplessness, night cries. Slight loss of weight, poor appetite, constipation. Irritable. Mother not aware of infection.	Red blood cells, 4,100,000 per c.mm. White blood cells, 16,000 per c.mm. 29.2 26.1 11.0 33.0 0.6 70.0						Complete relief of symptoms after one week.
12	Female 8	U. S.	Oxyuris ver- micularis	Irritable. Rectal irritation, genital pruritis. Appetite capricious, bowels constipated. Worms seen by mother.	56.0	24.1	13.0	6.2	0.3	75.0	Improvement. Relief of symptoms in one week. Lost track of.

per cent.) harbored intestinal worms. Five of these 80 children were infected with two species of parasite, which gives a total of 85 infections. Thirty-one (11.07 per cent.) of the children were infected with *Trichuris trichiura*, 23 (8.21 per cent.) harbored *Oxyuris vermicularis*, 20 (7.14 per cent.) were infected with *Hymenolepis nana*, 6 cases (2.14 per cent.) harbored *Ascaris lumbricoides*, and *Tenia saginata* was found in 5 cases (1.78 per cent.).

In the double infections, *Hymenolepis nana* and *Trichuris trichiura* were present together in 2 cases, *Hymenolepis nana* and *Oxyuris vermicularis* in 1 case, and *Ascaris lumbricoides* and *Oxyuris vermicularis* were associated in 2 cases. Out of the total of 85 infections, *Trichuris trichiura* occurred in 36.47 per cent., *Oxyuris vermicularis* in 27.05 per cent., *Hymenolepis nana* in 23.52 per cent., *Ascaris lumbricoides* in 7.05 per cent., and *Tenia saginata* in 5.88 per cent.

The only recent statistical study of the intestinal worms of children in this country that I have been able to find is that of Stiles and Garrison.<sup>1</sup> These investigators examined the feces of 123 children under fifteen years of age, and found evidence of infection with intestinal worms in 26 cases (21.14 per cent.). *Trichuris trichiura* was present in 16 cases (13.01 per cent.), *Oxyuris vermicularis* in 2 cases (1.63 per cent.), *Ascaris lumbricoides* in 1 case (0.81 per cent.), and *Hymenolepis nana* in 6 cases (4.88 per cent.). There were no cases of infection with *Tenia saginata* in children.

The important features of my cases will be considered under the headings of the different parasites.

**TRICHURIS TRICHIURA** (*Trichocephalus dispar*, *T. hominis*, *T. trichiura*, the whipworm). Table II; Cases VII and IX, Table I. In the first group of examinations (Table I) there were 2 instances of infection with this parasite; in the second group, 31. In 2 cases of the second group this parasite was found in association with *Hymenolepis nana*.

*Symptomatology.* None of the cases in the second group presented symptoms due to the whipworm, and 1 of the 2 cases in the first group must be excluded, since the relationship of the symptoms to the presence of the parasite is unproved. There seems little doubt that the symptoms in the other case (IX, Table I) were due to the presence of the parasite. This patient, a boy, aged seven years, had lost weight for nearly a year, and during this time he had become pale and listless. Appetite, sleep, and bowel movements were normal. There was slight puffiness of the lower eyelids, and the blood showed a moderate grade of secondary anemia with the presence of nucleated red cells (normoblasts). The number of red cells was 3,100,000 per cubic millimeter, and the hemoglobin 40 per cent. The urine was negative. The usual tonics (iron, arsenic,

<sup>1</sup> Bull. No. 28, Hyg. Lab. U. S. Pub. Health and Marine Hosp. Serv., 1906.

and cod-liver oil) had been administered over a period of four months, with little benefit. Numerous ova of the whipworm were discovered in the feces, and the patient was treated on the basis of this finding. Twice a week for three weeks thymol (12 grains) was given in divided doses, and during this time the feces were frequently examined to determine the number of ova. After the first two treatments the number of ova greatly diminished, and then remained stationary. Irrigations of salt water, quassia, and garlic infusions were given with little appreciable effect. Benzine irrigations were given according to the recommendation of Hemmeter,<sup>2</sup> with the result that the feces became free from ova. No other treatment was used, and no change was made in the mode of life. The improvement was marked. At the end of eight weeks the patient had gained three and a half pounds and the hemoglobin had risen to 65 per cent. Owing to the distance at which the patient lived it was impossible to examine the feces to determine the number of parasites expelled. The mother, however, noted the parasites, and specimens were brought for verification.

This case is given in some detail, because the whipworm is in most instances a harmless parasite. In some cases, however, when present in large numbers, this parasite may give rise to severe symptoms, and may even cause death. This is not surprising, since Askanazy<sup>3</sup> has shown that the intestinal canal of this parasite contains blood pigment, and Guiart and Garin<sup>4</sup> found that the stools of those infected reacted positively to the Weber test for occult blood. Becker<sup>5</sup> has collected cases from the literature in which the whipworm was responsible for definite symptoms. The symptoms were frequently intestinal: diarrhoea, often with bloody stools, vomiting, abdominal pain, etc. In other cases nervous symptoms, such as dizziness and severe headaches, occurred. Becker reported a case of secondary anemia which closely resembles the case cited. Theodor<sup>6</sup> reported a case of progressive pernicious anemia in a boy, aged eleven years, whose stools contained numerous ova of *T. trichiura*. Somewhat similar cases have been reported by Ostrovsky<sup>7</sup> and by Sandler.<sup>8</sup>

*Blood Examinations.*<sup>9</sup> The published reports on this subject

<sup>2</sup> Diseases of the Intestine, 1902, p. 552.

<sup>3</sup> Deut. Archiv f. klin. Med., 1896, lvii, 104.

<sup>4</sup> Semaine méd., xxix, No. 35.

<sup>5</sup> Deut. med. Woch., June 26, 1902, p. 648.

<sup>6</sup> Archiv f. Kinderheilk., 1900, xxviii.

<sup>7</sup> Abst. New York Med. Jour., 1900, lxxii, 826.

<sup>8</sup> Deut. med. Woch., 1905, xxxi, 95.

<sup>9</sup> The differential counts were made from blood smears stained with Wright's stain, and 500 to 1000 cells were counted. Most of the hemoglobin estimations were made with the Sahli hemometer. The instrument used had been standardized by the blood of normal children. The average percentage of hemoglobin in children between two and six years was 70 to 80 per cent; in children six to twelve years of age, 75 to 85 per cent. A few of the hemoglobin estimations were made with the Talquist scale, which I have found to give readings approximately the same as the Sahli instrument. When counts of the blood cells were made, the Thoma-Zeiss apparatus was used.



TABLE II.—TRICHIURIS TRICHIURA CASES FROM 280 CONSECUTIVE EXAMINATIONS.

No.	Sex and age.	Nationality.	Parasites.	Symptoms.	Blood Examination.						Result.	
					Polynuclear neutro- phile cells. Per cent.	Lymphocytes. Per cent.	Large mononuclear cells. Per cent.	Eosinophile cells. Per cent.	Basophile cells. Per cent.	Hemoglobin. Per cent.		
1	Female 3	U. S.	....	None	No apparent leukocytosis	52.3	31.5	12.0	3.5	0.5	60.0	....
2	Male 3	Russia	....	None	44.1	37.3	15.0	2.1	0.5	70.0	....	
3	Male 4	U. S.	....	None								....
4	Male 4	U. S.	....	None								....
5	Male 5	U. S.	....	None	No apparent leukocytosis	51.0	28.0	16.0	3.1	0.6	70.0	....
6	Female 5	U. S.	....	None	Slight leukocytosis (?) (estimated)	49.0	32.7	16.5	1.7	—	60.0	....
7	Male 5	Italy	....	None								....
8	Male 6	U. S.	....	None	No apparent leukocytosis	55.5	20.6	19.1	4.5	0.1	80.0	....
9	Female 7	U. S.	....	None								....
10	Female 7	Ireland	....	None	No apparent leukocytosis	46.0	41.2	9.2	3.5	—	75.0	....
11	Female 7	U. S.	....	None	No apparent leukocytosis	51.0	34.1	10.0	2.8	—	75.0	....
12	Male 7	U. S.	....	Double infection, H. nana and T. dispar. No symptoms referable to helminthiasis. See No. 15, Chart IV								....
13	Female 8	U. S.	....	None	No apparent leukocytosis	49.1	22.4	24.0	3.2	0.5	80.0	....
14	Male 8	U. S.	....	None								....

15	Male 8	U. S.	....	None	Slight leukocytosis (?) (estimated) 53.4 24.1 16.8 4.4 0.8 70.0	....	....
16	Male 8	Ireland	....	None		....	....
17	Male 8	U. S.	....	None		....	....
18	Female 9	U. S.	....	None	65.3 19.2 10.0 4.9 — 75.0	....	....
19	Female 10	Germany	....	None	No apparent leukocytosis — 70.0	....	....
20	Male 10	U. S.	....	None	63.0 20.0 13.5 3.2 — 70.0	....	....
21	Male 10	U. S.	....	None	No apparent leukocytosis 0.4 65.0	....	....
22	Female 10	Sicily	....	Double infection, <i>H. nana</i> and <i>T.</i> dispar. No definite symptoms. See No. 19, Chart IV	55.5 19.8 22.0 2.2 0.4 65.0	....	....
23	Male 10	U. S.	....	None	No apparent leukocytosis 44.3 35.0 18.0 1.9 0.3 65.0	....	....
24	Male 10	U. S.	....	None		....	....
25	Male 10	U. S.	....	None		....	....
26	Female 11	U. S.	....	None		....	....
27	Male 11	U. S.	....	None	No apparent leukocytosis 46.1 33.2 13.2 6.4 0.9 65.0	....	....
28	Male 12	U. S.	....	None	No apparent leukocytosis 65.0 20.0 12.0 2.4 0.4 75.0	....	....
29	Female 12	U. S.	....	None		....	....
30	Female 12	U. S.	....	None	70.0 19.2 6.0 4.1 0.1 75.0	....	....
31	Male 12	U. S.	....	None		....	....

indicate that the whipworm rarely produces an increase in the percentage of the eosinophile cells. In the case reported by Becker the eosinophile cells were 2 per cent. French and Boycott<sup>10</sup> made differential blood counts on 26 patients who harbored this parasite, and found that the eosinophile cells were not increased. One case showed 5.5 per cent. of eosinophile cells, but even though 5 per cent. is taken as an arbitrary standard, this single observation is of little importance. Brown<sup>11</sup> mentions that in no less than 10 or 12 cases in which *Trichocephalus hominis* appeared alone, the percentage of eosinophile cells rarely fell below 5. No cases are cited, nor are the exact percentages of the eosinophile cells given. Naegeli<sup>12</sup> has found eosinophilia in whipworm infections. Manson<sup>13</sup> says that in some few cases eosinophilia was found in persons infected with this parasite, but that this does not appear to be the rule. I have made differential counts in 18 cases of single infection with the whipworm, and in only 1 case was the percentage of eosinophile cells above 5 (XXVII, Table II). In this case the eosinophile cells were 6.4 per cent. Two other children from the same family harbored the threadworm, and it is quite possible that the patient in question was infected with threadworms, which were not detected in the routine examination.

*Treatment.* It is fortunate that this parasite so rarely causes symptoms, for the treatment is notoriously unsatisfactory. Stiles<sup>14</sup> cites an instance in which 300 parasites were expelled by thymol. In experimental infections in dogs Stiles and Pfender found thymol of little value. In the single case in which treatment was given by me, the number of parasites seemed to decrease under treatment with thymol, judging by the number of ova found in the stools, and the ova finally disappeared with the use of benzine irrigations.

*OXYURIS VERMICULARIS* (the threadworm, pinworm, or seatworm). Table III; Cases III, IV, V, VI, VIII, X, XI, and XII, Table I. In the consecutive examinations there were 23 cases of infection with this parasite, but I am of the opinion that more children harbor this worm than is indicated by these figures. It is well known that the ova of this parasite are not frequently found in the feces, but that the female worms are more often present. It is possible that when only a comparatively small number of worms are harbored they may be passed intermittently, and in consequence not be found in a single examination. Moreover, the small specimens of feces obtainable for these examinations may not have contained the worms, even though they were being passed at the time. Although in most instances a calomel purge was given before

<sup>10</sup> Jour. Hyg., 1905, v, 274.

<sup>11</sup> Bost. Med. and Surg. Jour., cxlviii, 583.

<sup>12</sup> Blutkrankheiten u. Blutdiagnostik, von Veit, Leipzig, 1908.

<sup>13</sup> System of Medicine, Albutt and Rolleston, 1907, vol. ii, part ii, p. 908.

<sup>14</sup> Modern Medicine, Osler and McCrae, 1907, i, 604.

obtaining the specimens of feces, three of the charted cases show how easily these worms may be overlooked. In Case IV, Table III, the presence of this worm was not suspected, but two pregnant female oxyurides were found in the feces after treatment for *H. nana*. Similarly, in Cases V and XVI, threadworms were discovered in the feces after the administration of santonin in the treatment for ascariis. The autopsy records of Still<sup>15</sup> are interesting, as showing the frequency of this worm. Out of 200 consecutive autopsies performed at the Great Ormond Street Hospital, in London, Still found the threadworm in 32 of 100 children between two and ten years of age.

*Symptomatology.* In 6 cases from the second group of examinations the threadworm was present without giving rise to symptoms (I, IV, V, VII, XV, and XVI, Table III). In one of these cases (XV) the child had previously suffered from symptoms, but none were present at the time of examination. The irritative symptoms produced by the nocturnal wanderings of these worms usually leads to their detection, but when local symptoms (rectal irritation, genital pruritus, etc.) are absent, the infection may not be suspected. In 4 cases from the first group of examinations, and in 5 of 17 children from the second group, who suffered from symptoms, the mother was not aware of the infection.

The most frequent symptoms referable to the threadworm are those of irritative nature due to the migration of the pregnant female worms. In this class is the genital pruritis and the rectal irritation. The vulvitis and masturbation in Case V, Table I, were probably of this origin, and both of these symptoms disappeared after appropriate treatment. Loss of weight, anemia, and headache are not infrequent symptoms, and may form the complaint for which the child is brought to the physician. This fact has been pointed out by Still.<sup>16</sup> The reflex nervous disturbances produced by this parasite are of importance. Restlessness at night, grinding of the teeth, night cries, and general irritability are particularly frequent. Cases are reported in which the threadworm may be responsible for convulsions or choreiform movements. Holt<sup>17</sup> cites a case in which threadworms were the probable cause of chorea. Gastro-intestinal symptoms are rather common. Still<sup>18</sup> has called particular attention to pain in the lower part of the abdomen and right iliac fossa as a symptom in Oxyuris infections. Sometimes the pains are referred to the umbilical region. Ashhurst<sup>19</sup> has recently reported a case in which, on operation for appendicitis, the appendix was found to contain numerous oxyurides. Cullhane<sup>20</sup> has reported

<sup>15</sup> Brit. Med. Jour., 1899, i, 898.

<sup>16</sup> Common Disorders of Childhood, 1909.

<sup>17</sup> Diseases of Infancy and Childhood, 1909.

<sup>18</sup> Common Disorders of Childhood, 1909.

<sup>19</sup> AMER. JOUR. MED. SCI., October, 1909, p. 583.

<sup>20</sup> Jour. Amer. Med. Assoc., 1910, liv, 48.

TABLE III.—CASES OF INFECTION WITH OXYURIS VERMICULARIS. FROM 280 CONSECUTIVE EXAMINATIONS.

No.	Sex and age.	Nationality.	Parasites.	Symptoms.	Blood Examination.						Result.
					Polynuclear neutro- phile cells. Per cent.	Lymphocytes. Per cent.	Large mononuclear cells. Per cent.	Eosinophile cells. (Per cent.	Basophile cells. Per cent.	Hemoglobin. Per cent.	
1	Male 3	U. S.	....	None due to helminthiasis. Mother not aware of infection	No apparent leukocytosis 46.7	32.2	16.2	4.2	0.3	79.0	Recovery.
2	Female 3	U. S.	....	Restless at night, grinds teeth. Intense itching of genitals and nose. Very pale, poor appetite, bowels normal, puffiness of lower eyelids. Mother has noticed worms for three weeks	Moderate leukocytosis (estimated)	0.3	myelocytes				
3	Female 3	U. S.	....	Restless at night, genital and nasal pruritis. Appetite and bowel movements normal. Child pale and thin. Mother has seen worms at intervals for one year	27.7	47.4	14.6	8.7	0.1	60.0	Recovery.
4	Male 4	U. S.	....	Double infection, Oxyuris vermicularis and H. nana. Symptoms probably due to latter. See No. 9, Chart IV	No apparent leukocytosis 36.0	46.3	16.6	0.95	—	65.0	
5	Male 4	U. S.	....	Double infection, scaris and Oxyuris vermicularis. Symptoms probably due to former. See No. 1, Chart V	No apparent leukocytosis 37.3 44.1 15.0 2.1 0.5 55.0						Two threadworms were found in the feces after treatment for H. nana.
6	Male 4	U. S.	....	Symptoms at intervals for three years. Genital and nasal pruritis. Night cries. Child pale and thin. Appetite poor when symptoms are present. Bowels regular. Mother aware of infection							One threadworm found in feces after treatment for A. lumbricoides. Improvement. Lost track of after twelve days.
7	Male 5	Italy	....	No apparent symptoms	No apparent leukocytosis 44.6 38.1 13.0 3.2 0.2 — Blood examination not obtained						Lost track of. Treatment not given.
8	Female 5	U. S.	....	Child pale, slight loss of weight, night cries. Appetite capricious, bowels regular. Mother not aware of infection							
9	Female 5	U. S.	....	Has not been well in two years. Flatulency; belches much gas after meals. Nausea. Cries out and jumps during sleep. Appetite poor, bowels normal. Mother has seen worms at intervals during two years	Red blood cells, 3,600,000 per c.mm. White blood cells, 5000 per c.mm. Thoma-Zeiss apparatus 57.5 27.7 14.0 0.2 0.5 40.0						Improvement with treatment. After two weeks symptoms had almost disappeared, hemoglobin, 50 per cent. Hemoglobin, 60 per cent. one month later.
10	Female 5	Ireland	....	Rectal irritation, genital and nasal pruritis. Restless at night, grinds teeth. Appetite and bowels normal. Mother has seen worms for three weeks	Slight leukocytosis (estimated) 36.1 42.0 13.4 7.1 0.2 65.0						Recovery.

11	Female 5	U. S.	....	None referable to helminthiasis. Mother had not seen worms	No apparent leukocytosis 69.3 14.8 13.1 1.9 0.6 70.0	Improvement with treatment.
12	Male 6	U. S.	....	One month. Itching of nose and genital region. Very restless at night, grinds teeth. Appetite and bowels normal. Mother had seen worms	No apparent leukocytosis 50.4 26.2 12.2 9.0 0.3 —	Recovery.
13	Male 6	U. S.	....	Restless at night. Rectal irritation. Genital and nasal pruritis. Appetite excessive. Bowels normal. Mother had seen worms	Slight leukocytosis (estimated) 26.4 49.0 13.2 10.5 0.6 —	Relief of symptoms by treatment.
14	Male 6	Ireland	....	Restless at night, night cries. Occasional attacks of right-sided abdominal pain. Bowels normal. Appetite capricious. Mother has seen worms for three weeks	No apparent leukocytosis 39.3 40.5 11.0 6.1 1.2 70.0	
15	Female 6	U. S.	....	No symptoms at time of examination. Mother noticed worms six months previously, at which time treatment was given for three weeks	Blood not examined	
16	Female 6	U. S.	....	Double infection, A. lumbricoïdes and O. vermicularis. Child pale and sparsely nourished. No definite symptoms	No apparent leukocytosis 42.0 40.2 14.3 1.8 0.5 70.0	Two oxyurides discovered in the feces after treatment for ascariis.
17	Male 7	Russia	....	Loss of weight. Pale. Child very fidgety, irritable. Attacks of nausea, no vomiting. Appetite capricious, bowels regular. Mother not aware of infection	Blood not examined	Relief of symptoms by treatment. Time of observations, three weeks.
18	Female 7	U. S.	....	For one month has complained of slight pain in right iliac fossa. Loss of appetite, loss of weight. Mother not aware of infection	Number of leukocytes apparently normal 60.3 16.1 12.0 9.3 1.0 60.0	Recovery.
19	Male 7	Germany	....	Restless at night, night cries. Very nervous and irritable. Constipated, appetite poor. Worms observed by mother	Leukocytes 16,000 (estimated) 60.1 18.0 6.0 13.1 2.0 70.0	Recovery.
20	Male 7	U. S.	....	Restless at night, grinds teeth. Genital pruritis. Appetite normal, bowels regular. Mother not aware of infection	Slight leukocytosis (estimated) 55.9 17.6 17.6 7.4 0.9 —	Lost track of.
21	Female 8	U. S.	....	Restless at night. Rectal irritation. genital and nasal pruritis (intense). Occasional abdominal pains. Appetite poor, bowels regular. Worms seen by mother	Moderate leukocytosis (estimated) 46.0 16.0 22.3 14.0 1.1 65.0	Recovery.
22	Male 11	U. S.	....	Nauseated after eating for one month. Frequent headaches. Bowels regular. Appetite poor. Mother not aware of infection	No apparent leukocytosis 50.0 22.0 20.3 7.1 0.03 70.0	Relief of symptoms after two weeks treatment. Lost track of.
23	Male 11	U. S.	....	Talks in sleep. Occasional night cries. Appetite excessive. Genital pruritis. Worms seen by mother. Has been troubled with threadworms off and on for three years	No apparent increase in number of leukocytes 45.0 39.0 9.7 6.0 0.2 65.0	Improvement for three weeks. Lost track of.

a similar case, and considers that the oxyurides were the cause of the appendicitis. Still<sup>21</sup> noted thickening and swelling of the appendix in some of his autopsies.

Pains in the lower part of the abdomen or right iliac fossa were present in 4 of my cases. The pains caused considerable annoyance, and in 1 case were of moderate severity. In these cases the temperature was normal and tenderness on palpation or muscle spasm were never elicited. The appetite was poor in 11 cases, capricious in 5, excessive in 2, and normal in 7 cases. In 1 case flatulency and nausea were complained of; in another, nausea alone. Diarrhœa, with blood and mucus in the stools, may be produced by this parasite. Diarrhœa was not a symptom in any of my cases, but constipation was frequent.

*Blood Examinations.* Differential blood counts were made on 22 patients who suffered from symptoms due to *Oxyuris vermicularis*, and in 17 the eosinophile cells were above 5 per cent. The percentage of the eosinophile cells varied greatly, and was between 6 and 10 per cent. in 12 cases, between 10 and 20 per cent. in 4 cases, and above 20 per cent. in 1 case. The eosinophile cells were not increased in 5 of the cases showing symptoms. Three of these cases (III, VI, and IX, Table III), from the second group of examinations, gave a history of infection with the threadworm for one, three, and two years, respectively, and the hemoglobin percentage in all 3 was low. Case IX showed a moderate grade of secondary anemia, with a red cell count of 3,600,000, a leukocyte count of 5000, and a hemoglobin percentage of 40. In Case III the hemoglobin was 65 per cent., in Case VI it was 55 per cent. In the two cases from the first group of examinations (V and VI, Table I) it was impossible to determine the duration of infection. In both cases the hemoglobin percentage was low. One patient, however (XXIII, Table III), gave a history of an infection of three years' duration, and the eosinophile cells were 6 per cent. Differential blood counts were made on 3 patients who did not suffer from symptoms, none of which showed an increased percentage of eosinophile cells.

Case VIII, Table I, is of particular interest, since this child was seen at the height of the infection, and the percentage of the eosinophile cells was followed during treatment. This patient suffered from rather pronounced symptoms, and at the time of admission the eosinophile cells were 33 per cent., the red blood cells 4,100,000 per cubic millimeter, the leukocytes 16,000 per cubic millimeter, and the hemoglobin 70 per cent. After treatment for five days the symptoms were much less severe, and the eosinophile cells were 13 per cent. Two weeks later the patient was free from symptoms, and at this time the eosinophile cells had fallen to 3 per cent.

<sup>21</sup> Brit. Med. Jour., 1899, i, 898.

In Boycott's<sup>22</sup> cases the eosinophile cells were above 5 per cent. in 8 out of 18 cases of threadworm infection in children. In the remaining 10 cases the eosinophile cells were not increased. No mention is made of the presence or absence of symptoms, but this investigator suggests that the presence of eosinophilia bears relation to the duration of infection.

*Treatment.* There are several observations, not generally recognized, which have direct bearing on the treatment for this parasite. An experiment of Grazzi<sup>23</sup> shows that the worms may arrive at maturity in the intestines during the last four or five weeks following a single infection. Since it is probable that fresh parasites constantly develop through auto-infection, the treatment should be continued for six weeks.

In the autopsies of Still<sup>24</sup> the worms were found in the appendix in 25 of the 38 cases which harbored *Oxyuris vermicularis*; in 6 cases the appendix seemed to be the only habitat.

The normal habitat of this worm is the cecum or appendix, and not the rectum and colon, as often stated. When the females become impregnated they migrate to the lower portions of the large intestine to discharge their ova. They often wander through the rectum and may pass out with the feces. Thus, the treatment should be given with two aims: first, to remove the worms which have migrated to the large intestine; and next, to expel those in the cecum or appendix. For the former purpose the usual irrigations of salt water, quassia, garlic, etc., are effective. As fluid injected per rectum may not always reach the cecum, internal treatment is of importance. Santonin is probably the most useful drug for this purpose, and is best given in doses of 1 to 3 grains, with the same amount of calomel, for three successive evenings. On the first and third mornings of treatment a cathartic should be given. This treatment may be repeated two or three times during the first three weeks.

During the first two or three weeks the irrigations should be given each evening, and from 6 to 20 ounces—depending on the age of the patient—can be given in each injection. Later, the irrigations may be given every alternate evening, and finally twice a week. Every effort should be made to prevent auto-infection, as this is a potent factor in keeping up the disease. At night a mild mercurial ointment (10 to 20 per cent.) may be applied around the rectum. The child should be prevented from scratching and from putting his fingers into his mouth.

A review of the tabulated cases shows how unsatisfactory the usual treatment may be. The mothers usually give the irrigations only during the period of active symptoms, or while worms are passed;

<sup>22</sup> Brit. Med. Jour., 1903, ii, 1267.

<sup>23</sup> Quoted by Manson, *System of Medicine*, Allbutt and Rolleston, 1907, vol. ii, part ii, p. 891.

<sup>24</sup> Brit. Med. Jour., 1899, i, 898.



often within two to four months the patients again show signs of severe infection. Although this parasite rarely, if ever, produces dangerous symptoms, yet the continual irritation which they set up may undermine the general health; this serves as a sufficient indication for thorough treatment.

*HYMENOLEPIS NANA* (*Tenia murina*, *Tenia nana*, the dwarf tapeworm). Table IV.<sup>25</sup> There were 20 cases, of infection with this parasite out of the 280 consecutive examinations. Nineteen of the patients were born in New York City; 1 patient was born in Sicily, and came to this country at the age of four years. This may have been an imported case, as the dwarf tapeworm is a comparatively common parasite in certain parts of Sicily.

Previous to the paper of Stiles,<sup>26</sup> in 1903, the dwarf tapeworm was not considered a common American parasite, but since this time a number of cases have been recognized in different sections of the country. In my investigations this parasite was the third in frequency, and there is every indication that it is a comparatively common, though perhaps unrecognized, parasite of children.

Seventy-nine, or 74.52 per cent., of the cases collected by Ransom<sup>27</sup> in 1904 were in children, and this parasite has been generally recognized as occurring most frequently in individuals under sixteen years of age.

No attempt will be made to give a description of the parasite, as this has been done in another paper. The dwarf tapeworm possesses certain points of similarity to the larger tapeworms, but differs in its minute size and the great number of the parasites usually present. The average length of the parasite ranges below 20 mm. (0.8 inch), and the worm contains from 110 to 200 segments. The number of parasites present in a single patient varies from a few to thousands. After treatment, 50 worms were recovered from the feces of one of my cases, and 60 from another; all of the other patients harbored more than 100 parasites, and one patient harbored many more than 2000. The number of parasites could be estimated in only 11 cases.

*Symptoms.* This parasite is of unusual medical interest, as a number of those infected suffer from symptoms referable to its presence. In Ransom's<sup>28</sup> analysis of the cases reported up to 1904 the most frequent symptoms were of the nature of nervous or gastrointestinal disorders. The nervous symptoms ranged from mild disturbances, such as nervousness, irritability, and restlessness at

<sup>25</sup> Fourteen of these cases (I, II, III, IV, VI, VII, VIII, XIII, XIV, XVI, XVII, XVIII, XIX, XX) have been published in the February number of the Archives of Pediatrics. In this paper the parasite and ova are described and the recent literature reviewed. Three other cases (V, IX, and XII) will be reported in the Jour. Amer. Med. Assoc., April, 1910.

<sup>26</sup> New York Med. Jour., 1903, lxxviii, 877.

<sup>27</sup> Bull. 18, Hyg. Lab. U. S. Pub. Health and Mar. Hosp. Serv., 1904.

<sup>28</sup> Ibid.

night, to severer manifestations, such as choreiform movements and definite convulsive seizures.

Among the symptoms referable to the gastro-intestinal tract, pain or paresthesia are common. The pain is colicky, is usually referred to the epigastrium, and occurs in paroxysms. These attacks of pain may be infrequent, but they often occur several times a day. Ransom<sup>29</sup> refers to one case in which there was epigastric tenderness in association with the pain. Abdominal paresthesia, in the nature of a sudden sinking sensation, or a sudden feeling of "goneness," is not uncommon in older children. Diarrhœa sometimes occurs. Deaderick<sup>30</sup> has reported 6 cases of dwarf tapeworm infection, all of which presented symptoms which were attributed to the presence of the parasite. According to him the most common symptoms were, in the order of frequency, nausea, vomiting, œdema, headache, abdominal pain, diarrhœa, dyspnœa, and convulsions.

In 8 of my cases there were no symptoms attributable to the dwarf tapeworm infection; in 12 cases there were well-marked symptoms, which disappeared or were greatly ameliorated after appropriate treatment. The symptoms were mild in 5 cases, moderate in 4, and rather severe in 3 cases.

The most common nervous symptoms were restlessness at night, night cries, grinding the teeth during the night, and general irritability. Numbness and tingling in one hand was a symptom in 1 case. One patient (IX) had three general convulsions, and the disappearance of all symptoms since the expulsion of *H. nana* indicates that the intestinal parasites were the exciting cause. Itching of the nose and genital region were not infrequent.

The most common gastro-intestinal symptom was epigastric pain. This symptom was present in 7 cases. The pain was colicky, and was most often mild and transient, but in 2 cases it was quite severe. There were no abdominal signs in these cases; tenderness on palpation, muscle spasm, or rigidity were never present. Diarrhœa was present in 1 case, attacks of nausea and vomiting in 1 case, and nausea unaccompanied by vomiting in 1 case. The appetite was increased in 3 cases, capricious in 1, decreased in 5, and apparently normal in the remaining 4 cases. One patient complained of a sudden sinking sensation, referable to the abdominal organs.

Pain in the lower limbs was complained of in 2 cases, and in 1 it was quite severe. Œdema of the lower eyelids was a sign in 2 cases. Loss of weight was a rather prominent feature in 3 cases; in the other cases, however, even in those with severe symptoms, emaciation was not evident.

<sup>29</sup> Bull. IS, Hyg., Lab. U. S. Pub. Health and Mar. Hosp. Serv., 1904.

<sup>30</sup> Internat. Clinics, 1909, iv; Jour. Amer. Med. Assoc., 1906, xlviii, 2087.

TABLE IV.—HYMENOLEPIS NANA. CASES FROM 280 CONSECUTIVE EXAMINATIONS.

No.	Sex and age.	Nationality.	Parasites.	Symptoms.	Blood Examinations.						Result.
					Poly-nuclear neutrophile cells. Per cent.	Lymphocytes. Per cent.	Large mononuclear cells. Per cent.	Eosinophile cells. Per cent.	Basophile cells. Per cent.	Hemoglobin. Per cent.	
1	Female 2	Russian parentage U. S.	....	None	28.4	28.9	30.0	2.4	—	80.0	About 200* parasites expelled by treatment. Feeces free from ova sixteen days later. Second examination, twenty-six days later, also negative.
2	Female 2	U. S.	....	Restless at night, grinding of teeth and night cries one month. Irritable.	Leukocytes 15,000 per c.mm. Thoma-Zeiss apparatus 57.7 17.5 16.0	6.5	1.2	65.0			About 150* parasites expelled by treatment. Disappearance of symptoms. Feeces free from ova sixteen and thirty-two days later.
3	Male 3	U. S.	....	Restless at night, grinding of teeth. Irritable. Frequent attacks of nausea and vomiting. Symptoms present six weeks	No apparent leukocytosis 42.5 41.5 8.0	6.9	0.5	70.0			About 100* parasites expelled. Eighteen days later very few ova still present in feces. Disappearance of symptoms.
4	Male 3	Italian parentage U. S.	....	None	No apparent leukocytosis 45.2 40.0 11.6	2.1	0.5	75.0			Feces free from ova eighteen days after treatment.
5	Male 3 1/4	Italian parentage U. S.	....	Has not been entirely well for one year. Symptoms worse past month. Severe attacks of epigastric pain. Very restless at night. Night cries. Appetite very poor. Bowels constipated. Listless, pale. Puffiness of lower eyelids	No apparent leukocytosis Red blood cells 3,000,000 per c.mm. Thoma-Zeiss apparatus 26.8 45.6 16.0	10.9	0.2	55.0			Many more than 2000* worms expelled by treatment. Improvement continuous from time of treatment. No ova found in feces twenty days after treatment.
6	Male 4	Russian parentage U. S.	....	Restless at night, increased appetite. Frequent attacks of epigastric pain. Nasal pruritus	White blood cells 14,000 per c.mm. Thoma-Zeiss apparatus 60.0 18.0 12.8	9.0	0.1	70.0			Disappearance of symptoms after treatment. 150 to 200* parasites expelled. Very small number of ova in feces three weeks later.
7	Female 4	U. S.	....	For two months nocturnal enuresis and genital and nasal pruritus. Appetite excessive, bowels normal	Leukocytes 16,000 Thoma-Zeiss apparatus 48.0 21.5 20.0	8.1	0.5	70.0			Disappearance of symptoms three weeks after treatment. Twenty days after treatment no ova found in feces. Eosinophiles 3.1 per cent.
8	Female 5	Italian parentage U. S.	....	Pale, frequent headaches, attacks of epigastric pain. Nervous, restless at night. Appetite poor, bowel movements normal	Leukocytes 13,000 per c.mm. Thoma-Zeiss apparatus 40.7 32.0 16.7	9.2	1.2	65.0			With exception of occasional headache is free from symptoms. Twenty days after treatment a very few ova were found in feces.

9	Male 5	U. S.	....	For two months, pale with loss of weight. Restless at night, night cries. Epigastric pain. Three general convulsions within past three weeks. Frequent attacks of diarrhea for about three months. Occasional attacks of epigastric pain. Restless at night, irritable. Appetite excessive. No definite symptoms	Slight leukocytosis (estimated) 45.0 40.3 7.6 7.0	70.0	No ova found in feces twenty days after treatment. Marked and progressive improvement since treatment. Improvement progressive after treatment. Feces contained no ova one month later.
10	Male 5	U. S.	....		Slight leukocytosis (estimated) 48.8 26.9 10.4 11.0 1.2	75.0	About 60* parasites expelled by treatment. No ova found in feces eighteen days later.
11	Female 5	U. S.	....	No definite symptoms	No apparent leukocytosis 53.6 27.3 13.0 3.5 0.5	75.0	About 300* worms expelled by treatment. Relief of symptoms after treatment. Feces free from ova twenty and thirty-six days after treatment.
12	Male 6	U. S.	....	For one year poor appetite, pale, frequent attacks of epigastric pain. Child very listless. Constipated, poor appetite. Symptoms much worse for past month	No apparent leukocytosis 49.9 22.5 13.8 13.0 0.4	60.0	Very small number of ova seen in feces three weeks after treatment.
13	Male 6	Italian parentage U. S.	....	None	No apparent leukocytosis 66.0 20.3 11.0 1.1	70.0	About 700* parasites expelled. Symptoms disappeared with exception of pains in limbs. Hb. 55 per cent. one month; 60 per cent. six weeks after treatment. Very small number of ova still found in feces.
14	Female 7	U. S.	....	For six months loss of weight. Pale, listless, easily tired. Frequent pains in lower extremities. Epigastric pain. Thin. Puffiness of lower eyelids. Appetite poor	Red blood cells, 3,200,000 per c.mm. White blood cells, 10,000 per c.mm. Normoblasts—microcytes Thomas-Zeiss apparatus 53.5 35.2 7.0 3.2 0.1	40.0	Very small number of ova in feces sixteen days after treatment. Gain in weight, disappearance of symptoms after treatment. Few ova found in feces three weeks later. At this time eosinophile cells were 2 per cent.
15	Male 7	U. S.	....	None. Double infection, H. nana and T. dispar	No apparent leukocytosis 56.7 26.4 9.6 5.0	75.0	About 200* parasites expelled. No ova seen in feces three weeks after treatment.
16	Male 9	Italian parentage U. S.	....	Loss of weight five weeks. Easily tired, sleep disturbed. Night cries, grinding of teeth. Genital and nasal pruritis. Appetite capricious	Red blood cells, 3,800,000 per c.mm. White blood cells, 24,000 per c.mm. Thomas-Zeiss apparatus 44.3 20.2 11.1 22.6 1.2	65.0	About 600* parasites expelled by treatment. Disappearance of symptoms. No ova found in feces sixteen and thirty-two days later.
17	Male 9	U. S.	....	No symptoms	No apparent leukocytosis 35.6 32.8 27.5 2.2 0.3	75.0	Very small number of ova in feces sixteen days after treatment.
18	Female 10	Russian parentage U. S.	....	Thin, nervous child. Nausea, sudden sensation of abdominal depression. Numbness and tingling in right hand. Pains in right thigh. Poor appetite. Loss of weight	Red blood cells, 4,100,000 per c.mm. Leukocytes, 16,000 per c.mm. Thomas-Zeiss apparatus 50.7 21.2 20.5 7.2 0.2	60.0	About 50* parasites expelled. No ova found in feces sixteen days and one month after treatment.
19	Female 10	Sicily	....	Rather thin. No definite symptoms. Double infection with H. nana and T. dispar	No apparent leukocytosis 42.2 40.8 14.8 2.7	70.0	
20	Female 11	U. S.	....	None	No apparent leukocytosis 42.0 31.2 22.5 4.0 0.3	80.0	

\* The numbers given represent the intact worms and parts consisting of nearly the whole worm. The parasites become broken up, and an exact count is impossible. The figures are probably too low. The number of parasites could be estimated in only 11 cases. In the other cases, none or only a small portion of the feces was preserved after treatment.

*Blood Examinations.* The blood examinations present points of especial interest. With a single exception, the percentage of eosinophile cells was increased in the patients who suffered from symptoms. The exceptional case was one of rather long standing infection with pronounced secondary anemia. The eosinophile cells were between 6 and 10 per cent. in 7 cases, between 10 and 20 per cent. in 3 cases, and above 20 per cent. in 1 case. The eosinophile cells were above 5 per cent. in only 1 of the cases without symptoms, and in this case the eosinophile cells were 5.2 per cent. The hemoglobin was determined in all cases, and in a number the percentage was below normal. The red blood cells were counted in 4 cases (V, XIV, XVI, and XVIII); and in all a secondary anemia was present. The degree of anemia may be characterized as mild in 1 case, moderate in 2, and rather severe in 1 case. In 1 case microcytes and normoblasts were present in the blood. In a number of the cases with eosinophilia the number of leukocytes seemed to be increased.

A case of infection with *Hymenolepis nana* is cited by Bücklers,<sup>31</sup> in which the eosinophile cells were 7 per cent. No mention is made in this case of the presence or absence of symptoms. Deaderick<sup>32</sup> has reported 6 cases of dwarf tapeworm infection which showed an eosinophilia of 11.5, 15, 9, 26, 8.2, and 7.8 per cent., respectively. All of these patients had symptoms apparently due to the parasites.

*Treatment.* Oleoresin of male fern is the remedy generally recommended, and is quite effective. Before the administration of the anthelmintic it is desirable to have the intestinal canal as empty as possible. To accomplish this the diet should be restricted to easily digested food for several days and a cathartic given each day. On the evening before the specific treatment a cathartic should be given; the oleoresin of male fern should be administered the following morning. It is of importance that the remedy be fresh, and it is best administered on an empty stomach. The dose will naturally vary with the age of the patient; from  $\frac{1}{2}$  to 1 dram is sufficient, and has, in my experience, been entirely harmless. It is best to give the male fern in three to five doses, administered at half-hour intervals. One-half hour after the last dose of male fern a brisk saline purge should be given.

A single treatment is not always sufficient, but its effectiveness can be determined by a later examination of the feces for ova. When worms are left in the intestinal canal, or develop after treatment, the ova usually reappear after an interval of about fifteen days.

*ASCARIS LUMBRICOIDES* (the common roundworm, the eelworm). Table V; Cases I and II, Table I. In the first group of examina-

<sup>31</sup> Münch. med. Woch., 1894, xli, 22 and 47.

<sup>32</sup> Jour. Amer. Med. Assoc., 1906, xlvii, 2087; Internat. Clinics, 1909, iv.

TABLE V.—ASCARIS LUMBRICOIDES. CASES FROM 280 CONSECUTIVE EXAMINATIONS.

No.	Sex and age.	Nationality.	Parasites.	Symptoms.	Blood Examinations.						Result.
					Polynuclear neutrophils. Per cent.	Lymphocytes. Per cent.	Large mononuclear cells. Per cent.	Eosinophiles. Per cent.	Basophile cells. Per cent.	Hemoglobin. Per cent.	
1	Male 4	U. S.	....	Irritable for six weeks. Nasal pruritis, poor appetite. Very restless at night. See No. 5, Chart II	46.2	32.0	10.5	9.0	1.2	65.0	Expulsion of one ascaris. One threadworm in feces after treatment. Still pale, relief of other symptoms.
2	Male 5	U. S.	....	Pale, restless, poor appetite. Occasional attacks of nausea and vomiting	50.5	31.0	9.6	6.5	0.5	70.0	Expulsion of one roundworm. Relief of symptoms.
3	Male 5	U. S.	....	Very nervous, restless at night, night cries. Pale, poor appetite. Two years ago was very ill. Jaundice at this time. Recovery (?) after expulsion of roundworm	45.5	26.2	18.7	9.2	0.2	70.0	Improvement after expulsion of one roundworm.
4	Male 6	U. S.	....	None	Slight leukocytosis (estimated)						Untreated. Lost track of.
5	Female 6	U. S.	....	None. See No. 16, Chart II	59.9	32.1	4.9	2.4	0.4	80.0	Expulsion of one roundworm.
6	Female 7	Italian parentage U. S.	....	Pale, poor appetite, restless at night	42.0	40.2	14.3	1.8	0.5	70.0	Two threadworms found in feces after treatment.
					64.2	22.0	6.1	6.9	—	70.0	Expulsion of one roundworm. Improvement.

tions (Table I) there were 2 cases of infection with this parasite; there were 6 cases (2.14 per cent.) in the 280 consecutive examinations.

The 2 cases from the first group are of sufficient interest to give in some detail. In the first case, the onset of the illness was sudden, with vomiting and loss of appetite. The child was very restless at night, and would frequently awake and cry out as if in pain. For ten days these symptoms continued; the evening temperature ranged from 101° to 102° F., and the respirations and pulse were proportionately increased. The patient was thoroughly examined, but nothing could be found to account for the symptoms. On the tenth day of the illness a blood count showed the presence of an eosinophilia (12.1 per cent.). This led to an examination of the stools, and the ova of ascaris were found in great numbers. The expulsion of a lumbricoid worm by santonin was followed by disappearance of all symptoms. An almost identical case is cited by Still.<sup>33</sup>

The symptoms in the other case (Table II), were less acute. For three months the patient had been irritable, pale, and had lost weight. At the time of admission he had an attack of jaundice; the skin, sclerotics, and mucous membranes were distinctly yellow. The stools were colorless, and the urine contained bile pigments. At this time the eosinophile cells were 12.6 per cent., and the ova of *A. lumbricoides* were found in the feces. After treatment, two ascarides were expelled. The jaundice lasted for ten days; after its disappearance the other symptoms improved, and the child began to gain in weight. This patient had passed a roundworm one month previous to the onset of the recorded illness.

Two of the 6 cases from the consecutive examinations suffered from no symptoms referable to helminthiasis; 3 of the remaining 4 cases suffered from mild symptoms; in one case the symptoms were rather severe. The more pronounced symptoms in these cases were the ones commonly due to the presence of this worm: loss of color and weight, poor appetite, restlessness at night, and night cries. One patient (II) suffered from attacks of nausea and vomiting, which have not recurred since the expulsion of one lumbricoid worm.

The past history of Case III was rather interesting. Two years before admission the child had an acute illness, accompanied by fever and jaundice. According to the mother's story, recovery ensued immediately after the passage of one lumbricoid worm.

*Blood Examinations.* In the 2 cases without symptoms the eosinophile cells were not increased. In all of the cases with symptoms, including the 2 cases from the first group of examinations, there was a moderate degree of eosinophilia. The percentages of eosinophile cells varied from 6.2 to 12.6.

*Treatment.* with santonin is effective, the details of which are given in all of the text-books. Experiments have shown that it takes about one month for the development of this worm from the ovum to the sexually mature parasite. Therefore, in order to be sure of the thoroughness of the treatment, the feces should be examined for ova after one month.

*TENIA SAGINATA* (*T. mediocanellata*, the fat, or beef tapeworm). Table VI. This parasite was found in 5 cases (1.74 per cent.), and in 3 cases the segments had been seen by the mother, who was consequently aware of the infection. In 2 cases (II and III) the diagnosis was made by finding the ova in the feces, and later confirmed by the discovery of the segments.

*Symptomatology.* Two of the 5 patients suffered from no symptoms referable to the tapeworm. Two of the remaining 3 patients suffered from nervousness; 1 child had become quite irritable, and 1 was very restless during sleep. The appetite was at times excessive in 1 case; in 2 cases it was meagre. One patient suffered from frequent attacks of abdominal colic, and the pain was referred to the epigastrium. None of the patients showed signs of emaciation.

*Blood Examinations.* The blood was not examined in the 2 cases without symptoms. In the 3 patients who suffered from symptoms the percentage of the eosinophile cells was increased, and ranged from 7.1 per cent. to 13.2 per cent.

*Treatment.* The treatment followed in these cases was that given under *Hymenolepis nana*.

**GENERAL DISCUSSION.** *Symptomatology and Pathology.* The obscurity of the symptoms of helminthiasis and the irregularity with which they occur has led to uncertainty and confusion. It is well known that in many instances intestinal worms produce no appreciable effect, while in other cases they may be responsible for definite symptoms which are always deleterious and sometimes severe.

The occurrence of symptoms in infection with the common intestinal worms seems to be, to some extent, dependent on the number of the parasites present. This factor, however, can be of little importance with parasites, of which, as a rule, only a single worm or a small number of worms are harbored. The cases collected by Becker,<sup>34</sup> in which the whipworm was responsible for severe symptoms, were all infected with large numbers of the parasite. In my cases it was in instances in which many threadworms were being passed that the symptoms were most marked. As a rule, the cases of dwarf tapeworm infection which harbored the largest number of worms suffered the most noticeable effects. On the other hand, one finds numerous references in the literature which

<sup>34</sup> Deut. med. Woch., June 26, 1902, 648.



TABLE VI.—TENIA SAGINATA. CASES FROM 280 CONSECUTIVE EXAMINATIONS.

No.	Sex and age.	Nationality.	Parasites.	Symptoms.	Blood Examinations.						Result.
					Polynuclear cells. Per cent.	Lymphocytes. Per cent.	Large mononuclear cells and transitional cells. Per cent.	Eosinophiles. Per cent.	Basophile cells. Per cent.	Hemoglobin. Per cent.	
1	Female 6	U. S.	....	Very nervous and irritable. Appetite at times excessive. Good color, well nourished. Has passed segments for two years	Slight leukocytosis (estimated) 44.0 16.1 25.2 13.2 0.7 80.0						Expulsion of tapeworm. Head not found. Segments had not reappeared four months later. Freedom from symptoms.
2	Male 9	U. S.	....	No symptoms referable to tapeworm. Mother not aware of infection	Not made						Did not return for treatment.
3	Male 10	U. S.	....	No definite symptoms. Child pale, poorly nourished. Mother not aware of infection	Not made						Expulsion of tapeworm. Head not found. Not seen since two days after treatment.
4	Female 10	U. S.	....	Pale. Restless at night. Appetite poor. Has passed segments for one year. Child is very nervous	Moderate leukocytosis (estimated) 48.3 18.5 23.6 9.0 0.3 55.0						Expulsion of entire worm. Improvement.
5	Male 12	Armenian	....	Pale, poor appetite, frequent attacks of colic. Pain referred to epigastrium. Segments observed by mother for eighteen months	No apparent leukocytosis. 42.0 20.0 30.0 7.1 0.4 70.0						Expulsion of tapeworm. Head not found. Patient not seen since two weeks after treatment. Improvement.

show that large numbers of parasites may be harbored with no apparent discomfort to the host. Dehio<sup>35</sup> believes that "Bothriocephalus anemia" is only produced after the death or disease of the parasite, but even if this is true, it seems scarcely possible that this factor comes into play with the common helminth.

The age of the patient is of great importance, for it is well known that reflex nervous disturbances are more likely to occur in children than in adults. The species of parasite is of some importance, but in infections with all of the parasites considered in this paper symptoms are inconstant. There is no adequate explanation for this irregularity in the occurrence of symptoms, but it may be due to a definite predisposition on the part of some individuals, or the worms may excrete toxic substances only under certain conditions, of the nature of which we are ignorant. It is not improbable that both factors are of importance.

As to the ultimate cause of the symptoms of helminthiasis there is little positive knowledge and much speculation. There have been experiments which indicate that some parasites at least excrete toxic substances which may have an influence on the host, and clinical experience often lends support to this view. A case has recently been reported by Artaega<sup>36</sup> in which ascarides were the probable cause of profound hemolysis. On the other hand, there are symptoms the nature of which suggests an irritative action, such as diarrhoea and the local irritation produced by migrating oxyurides. Many of the nervous disturbances are probably reflex, due to the irritation set up by the worms.

It has been mentioned that the intestinal canal of the whipworm was found to contain blood pigment,<sup>37</sup> and that the feces of those infected with this parasite reacted to an occult blood test.<sup>38</sup> Autopsies have shown that the head of the dwarf tapeworm burroughs into the intestinal mucosa, and that considerable inflammation may be thus produced. Without undue speculation, it can be safely said that the present state of our knowledge indicates that the influence of the common intestinal worms is due to direct irritation, to the abstraction of blood, or to toxic substances excreted by the parasite.<sup>39</sup>

<sup>35</sup> Quoted by Emerson, *Clinical Diagnosis*, 1906, p. 359.

<sup>36</sup> *Abst. Jour. Amer. Med. Assoc.*, May 8, 1909.

<sup>37</sup> *Deut. Archiv f. klin. Med.*, 1896, lvii, 104.

<sup>38</sup> *Semaine méd.*, xxix, p. 35.

<sup>39</sup> No mention is made of the well-known mechanical effects due to the migration of *Ascarides*. The various means by which parasitic worms may produce injury is summarized by Stiles as follows: (1) Nourishment is taken which should go to the host; (2) blood is taken by the parasites as food; (3) mechanical pressure irritates or causes atrophy of organs or parts of organs; (4) natural channels may be obstructed; (5) the wandering of the parasites may cause irritation; (6) substances may be excreted which may have a toxic influence, and which may change the natural condition of the body fluids (blood); (7) injury to the intestinal mucosa or to the skin may form points of entry for bacterial or protozoan infections (Osler and McCrae, *Modern Medicine*, vol. i, 1907).

The most important symptoms of helminthiasis may be tabulated as follows:

- I. Gastro-intestinal symptoms.
  - (A) Nausea.
  - (B) Vomiting.
  - (C) Diarrhœa.
  - (D) Abdominal pain.
  - (E) Jaundice. Commonest in ascaris infections. May be due to duodenitis or to mechanical obstruction of a bile duct by a parasite. May occur in tapeworm infections.
  - (F) Abdominal paresthesia.<sup>40</sup>  
Sinking sensations, feeling of emptiness, sensation of "goneness," etc. Commonest in tapeworm infections.
  - (G) Disturbances of appetite.
    1. Increased appetite.
    2. Decreased appetite.
    3. Capricious appetite.
    4. Perverted appetite.
  - (H) Intestinal obstruction. (Ascarides.)
- II. Symptoms of nervous organs. (May be reflex or tonic?)
  - (A) Disturbances of sleep.
    1. Restlessness.
    2. Grinding of teeth.
    3. Night cries.
  - (B) Irritability, nervousness.
  - (C) Nasal pruritus.<sup>41</sup>
  - (D) Dyspnœa.
  - (E) Dizziness and vertigo.
  - (F) Choreiform movements.
  - (G) Convulsions.
  - (H) Paralysis. (Functional.)
- III. Symptoms referable to organs of special sense.
  - (A) Perversions of—
    1. Sight.
    2. Hearing.
    3. Taste.
    4. Smell.
  - (B) Pupillary changes.

<sup>40</sup> This is really a nervous symptom, but since the sensations are referred to the abdomen, it is placed in the above heading..

<sup>41</sup> The origin of this symptom is obscure. Its relationship to helminthiasis is doubted, probably because many children not harboring intestinal worms have the habit of picking or scratching the nose. Nasal itching, however, is mentioned by most authorities on helminthiasis, and appears in the statistics of Cobbold and Hirsch, on the symptoms of tapeworm infections.

#### IV. Symptoms referable to the skin or due to irritation of the skin or mucous membranes.

##### (A) Symptoms referable to skin.

1. Erythema.
2. Urticaria.

} *Ascaris*, tapeworms.

##### (B) Rectal irritation (*Oxyuris vermicularis*).

##### (C) Genital pruritus,<sup>42</sup> or irritation, which may lead to—

1. Vulvitis or vulvovaginitis.
2. Enuresis.
3. Masturbation.

} Usually in infections with *Oxyuris vermicularis*.

#### V. General symptoms.

##### (A) Loss of weight.

##### (B) Anemia.

*Blood Changes.* Müller and Reider,<sup>43</sup> in 1891, and Zappert,<sup>44</sup> in 1893, found an increase of the eosinophile cells in cases of uncinariasis. Following these observations, eosinophilia has been noted in infections with many varieties of parasitic worms. In the case of the more common and often harmless parasites the recorded observations show that eosinophilia may occur, but is inconstant.

In the blood counts made by Boycott<sup>45</sup> in cases of oxyuris infection, about two-fifths of the cases showed an eosinophilia. This inconstancy has been noted by other observers.

From his studies on uncinariasis, Boycott<sup>46</sup> is of the opinion that the presence and degree of eosinophilia is in inverse proportion to the duration of infection. He found in cases of hookworm infection that the eosinophilia gradually disappeared without the worm leaving the intestine. Ashford and King,<sup>47</sup> in their work on uncinariasis, found that there was no increase in the eosinophile cells in severe infections or in those of long standing associated with anemia.

These clinical observations find confirmation in the experimental work of Opie<sup>48</sup> on trichinosis. This investigator administered estimated numbers of the encysted embryos of *Trichina spiralis* to guinea-pigs, and observed the effect of the infection on the eosinophile cells. He found that the administration of a moderate number of trichinae produced eosinophilia, but when a severe infection was induced, the eosinophile cells decreased or disappeared, and death of the animal ensued.

<sup>42</sup> This symptom is probably not always due to local irritation, since it may occur in tapeworm infections. With the larger tapeworms the passage of segments may be the causative factor. This could hardly explain its occurrence in the case of the dwarf tapeworm, where the segments are extremely small and do not seem to be regularly passed.

<sup>43</sup> Deut. Archiv f. klin. Med., 1891, xlviii, 96.

<sup>44</sup> Zeitschr. f. klin. Med., 1893, xxiii, 227.

<sup>45</sup> Brit. Med. Jour., 1903, ii, 1267.

<sup>46</sup> Jour. Hyg., 1903, iii, 95; 1904, iv, 437.

<sup>47</sup> Amer. Med., 1903, vii, 391.

<sup>48</sup> AMER. JOUR. MED. SCI., 1904, exxvii, 477.

From the blood counts in my cases it seems that the occurrence of eosinophilia bears relation to the presence of symptoms and to the duration of infection. In other words, eosinophilia was generally absent in cases which presented no symptoms of helminthiasis (usually, but not always, light infections). Eosinophilia was usually present in cases which presented symptoms, with the exception of severe or long-standing infections. The degree of eosinophilia did not seem to bear any constant relation to the severity of the symptoms.

The above statements are not strictly applicable to the whipworm, since this parasite did not cause an increase of the eosinophile cells. On the other hand, it rarely causes symptoms. The significance of the percentages of the eosinophile cells found in children who harbor intestinal worms is, obviously, dependent on the percentages of these cells found in normal children.

It is often stated that in children the normal percentages of the eosinophile cells are much greater than those considered normal for adults. The investigations of Carstanjen<sup>40</sup> on children do not show that the percentage of these cells is uniformly high. They indicate, however, that the percentages may vary greatly in children of the same age. Thus, in children between four and five years of age, the eosinophile cells in one case were 0.75 per cent., in another 16.65 per cent. The eosinophiles were above 6 per cent. in 16 of the 55 children between two and thirteen years of age. The counts of Zappert<sup>50</sup> have practically the same significance; 16 of the 28 children between two and thirteen years of age showed an eosinophilia of more than 6 per cent. In one case, a child with chorea, the eosinophiles were 19.54 per cent. As shown in the reports of these writers, a number of the children suffered from various chronic disorders, and therefore cannot be considered entirely normal. The attempt to exclude helminthiasis is not mentioned in any of these investigations, and apparently was not made.

Boycott<sup>51</sup> found the eosinophile cells under 5 per cent. in 8 out of 10 normal and apparently "wormless" children. In one case the eosinophile cells were 5.2 per cent.; in another, 5.4 per cent. I have made differential blood counts on 20 apparently normal children who did not harbor intestinal worms—judging from an examination of the feces (Table VII); 14 of these children appeared normal, and complained of no symptoms; 6 were recovering from mild digestive disorders. In 18 cases the eosinophile cells were below 5 per cent., in 1 case they were 5 per cent., and in 1 case 6 per cent.

The possibility of an idiopathic eosinophilia in children cannot

<sup>40</sup> *Jahr. f. Kinderheilk.*, 1900, lii, 215, 233, and 684.

<sup>50</sup> *Ztschr. f. klin. Med.*, 1893, xxiii, 227.

<sup>51</sup> *Brit. Med. Jour.*, 1903, ii, 1267.

be excluded on the basis of this small number of examinations. The results, however, are of sufficient uniformity to indicate that in normal children—not harboring intestinal worms—the eosinophile cells are not frequently above 5 per cent. This question, however, is worthy of further study.

There have been a number of experiments which throw light on the cause of eosinophilia in infections with parasitic worms. Accumulation of eosinophile cells in the intestinal wall has been observed by Strong<sup>52</sup> and Yates<sup>53</sup> in postmortem examinations of fatal cases of uncinariasis. A local accumulation of eosinophile cells in the muscles containing encysted trichinæ has been observed by Brown,<sup>54</sup> Opie,<sup>55</sup> and others. Calamada<sup>56</sup> was able to produce eosinophilia in rabbits and guinea-pigs by the injection of a filtered aqueous extract of *Tenia saginata*.

TABLE VII.—THE PERCENTAGE OF EOSINOPHILE CELLS IN APPARENTLY NORMAL CHILDREN.

No.	Age Years.	Per cent. of eosino- phile cells.
1*	2	5.0
2†	2	2.8
3†	2	2.3
4†	3	3.9
5*	3	6.0
6†	3	4.3
7*	5	3.2
8†	5	0.9
9†	5	3.8
10*	5	2.1
11†	5	4.7
12†	6	1.2
13†	6	0.8
14*	6	0.01
15*	8	3.7
16†	8	4.0
17†	8	0.2
18†	10	1.6
19†	10	2.4
20†	11	3.5

\* Patients from private practice.

† Dispensary patients.

These experiments indicate that the parasites probably excrete substances which have a positive chemotactic influence on the eosinophile cells. Moreover, it is probable that the eosinophilia represents a reaction on the part of the organism, and that in severe or long-standing infections the power of producing eosinophile cells is gradually diminished.

The association of Charcot-Leyden crystals with eosinophilia has been observed in several diseases. These crystals frequently occur in the feces in helminthiasis, and their presence is of considerable

<sup>52</sup> Quoted by Opie.

<sup>54</sup> Jour. Exper. Med., 1898, iii, 315.

<sup>56</sup> Cent. f. Bakt. u. Parasit., 1901, xxx, 375.

<sup>53</sup> Johns Hopkins Hosp. Bull., 1901, xii, 366.

<sup>55</sup> AMER. JOUR. MED. SCI., 1904, cxxvii, 477.

diagnostic value. Charcot-Leyden crystals are probably derived from the eosinophile cells, so that their occurrence in the feces in helminthiasis would seem to represent a local eosinophilia.<sup>57</sup>

Bücklers<sup>58</sup> has noted the presence of Charcot-Leyden crystals in the feces of cases of helminthiasis showing eosinophilia. I examined the feces for Charcot-Leyden crystals in 14 cases with eosinophilia, and the result was positive in the following: in 1 of 6 cases infected with *H. nana*, in 4 of 6 cases infected with *O. vermicularis*, and in both of 2 cases infected with *T. saginata*.

In a number of my cases the large mononuclear and transitional cells were above the percentages usually given as normal. The apparent increase in these cells seemed of no especial significance, and had no relation to the presence of symptoms or to the severity of the infection. The percentage of basophile cells (mast cells) was frequently increased, and the increase was greatest in cases showing eosinophilia. This relationship, however, was not constant, and the mast cells were increased in several cases not showing eosinophilia.

The percentage of hemoglobin was low in many of the patients who suffered from symptoms. The anemia was more pronounced in the threadworm and dwarf tapeworm infections.

**DIAGNOSIS.** It seems hardly necessary to state that it is impossible to diagnosticate the presence of intestinal worms from the symptoms produced in the host. The symptoms of helminthiasis are usually obscure and are more often due to other causes.

The presence of *Tenia saginata* is usually indicated by the passage of segments, but, as previously shown, these may not be observed. The migration of oxyurides and the local symptoms produced often leads to their detection. The presence of ascarides may be indicated by the previous passage of a worm. Segments of the dwarf tapeworm are occasionally found in the stools, but they are so minute that they can only be recognized by means of a lens. Rarely the intact worms may be passed after the administration of a cathartic. The whipworm is rarely, if ever, found in the stools.

The easiest and only satisfactory diagnostic method is the examination of the feces for the parasites, their parts, or ova. It is best to administer a calomel purge before obtaining the specimen for examination, as by this means oxyuris is more likely to be detected. A number of methods of examination have been recommended, but I have found the following to be entirely satisfactory: A small portion of the feces (15 to 20 grams) is thoroughly mixed with sufficient distilled water to make a translucent mixture. This is well shaken, and a large drop is placed on a slide and covered with a cover-slip. By means of the mechanical stage eight to ten preparations are thoroughly examined. Two by three inch slides and

<sup>57</sup> Limasset, Thèse de Paris, 1901.

<sup>58</sup> Münch. med. Woch., 1894, xli, 22 and 47.

one by two inch cover-glasses are more convenient than the ordinary size, as more material can be examined in a single specimen. In conducting the microscopic examination, a moderate illumination is desirable, and it is best not to use a condenser. Transparent and colorless ova, such as those of the dwarf tapeworm, the threadworm, and hookworm, are likely to be overlooked if the illumination is too intense.

It is rather important that the feces be thoroughly mixed, since the ova of parasites inhabiting the upper intestinal tract are more likely to be found in the centre of the fecal mass, while the ova of other parasites are only discharged in the large intestine, and in consequence are more likely to be in the external layer. Scrapings from the rectum frequently give positive results with the threadworm when the examination of the feces is negative.

One finds rather frequent references to pseudo-ova, which may lead to confusion. These bodies are usually vegetable cells, which have a cell membrane and cellular or granular contents. After the ingestion of some of the common fruits—oranges, raspberries, bananas, etc.—these cells are frequently found in the feces. Starch granules and epithelial cells may occasionally have a superficial resemblance to ova. Although these bodies may be a source of confusion, yet their resemblance to true ova is only superficial. All danger of confusion is eliminated by familiarity with the appearance of the ova of intestinal worms. Absolute verification of the diagnosis may be obtained by recovery of the parasite.

To search for parasites the feces should be well diluted and poured into a flat vessel, the bottom of which has been painted black. By this means the worms can be easily recognized, and their species determined by microscopic examination.

If further argument were needed to show the importance of examining the feces for ova, it is only necessary to recall my statistics. The parasites which rank first (the whipworm) and third (the dwarf tapeworm) in frequency are never observed by the patients, but can only be detected by finding the ova on microscopic examination of the feces.

**PROPHYLAXIS.** With the exception of *Tenia saginata*, infection with the parasites dealt with in this paper results from the ingestion of ova. Infection with *Tenia saginata* occurs from ingestion of so-called "measley beef," that is, meat containing the cysticercus stage of this parasite. The tongue and muscles of mastication most often contain the cysticerci. The exclusion of all infected meat by rigid inspection is the best preventive measure. Heat destroys the embryos, and thorough cooking of infected meat will render it harmless. To prevent infection with the other parasites, it is important that infected cases should be thoroughly and promptly treated. Measures should be taken to prevent contamination of the water supply with the ova. To prevent infection of other



members of the family, rigid cleanliness should be observed, and the contamination of food or hands with the feces of infected persons guarded against. An experiment of Stiles<sup>50</sup> indicates that flies may be the carriers of the ova of the eelworm of hogs—a parasite closely related to the eelworm of man. It is possible that infection with the human parasite may be disseminated in this manner. The prophylaxis is obvious. It is possible that infection with the dwarf tapeworm may result from contamination of food with the feces of rats or mice infected with this worm. This gives another indication for the extermination of rats and mice. To prevent the spread of intestinal worms, it is only necessary to remember that the feces of those infected usually contain great numbers of the ova, and that the ingestion of a single ovum may lead to the development of an intestinal worm.

SUMMARY. 1. Twelve of 30 children who suffered from unexplained nervous or gastro-intestinal symptoms were found to harbor intestinal worms.

2. Consecutive examinations of 280 children showed that 80 (28.57 per cent.) harbored intestinal worms. Five of the children harbored two species of parasite, giving a total of 85 infections.

3. Thirty-one (11.07 per cent.) of the children harbored *Trichuris trichiura*, 23 (8.21 per cent.) harbored *Oxyuris vermicularis*, 20 (7.14 per cent.) harbored *Hymenolepis nana*, 6 (2.14 per cent.) were infected with *Ascaris lumbricoides*, and 5 (1.78 per cent.) with *Tenia saginata*.

4. Only 1 of 33 children infected with *Trichuris trichiura* (from both groups of examinations) suffered from symptoms.

5. Thirty-five of the 51 children infected with the other parasites (from the consecutive examinations) suffered from symptoms.

6. The eosinophile blood cells were not increased in cases infected with *Trichuris trichiura*.

6. In infections with the other parasites eosinophilia was usually absent when there were no symptoms due to helminthiasis. Eosinophilia was generally present in cases which presented symptoms of helminthiasis.

CONCLUSIONS. 1. Intestinal parasites are not infrequent among the children of the poorer classes of New York City.

2. Intestinal worms may be harbored without inconvenience to the host. On the other hand, symptoms may occur which are always deleterious, and sometimes severe.

These investigations were made on patients from the clinic of Dr. Thomas S. Southworth at the out-patient department of the Babies' Hospital, and from the service of Dr. Eli Long, at the New York University and Bellevue Hospital Medical College. I desire to express my appreciation for this privilege and for encouragement

<sup>50</sup> Modern Medicine, Osler and McCrae, 1907, i, 597.

in carrying out the work. I wish to acknowledge my indebtedness to Miss Eleanor Ketcham, visiting nurse to the children's clinic of the New York University and Bellevue Hospital Medical College, for valuable assistance in obtaining material and in following the cases.

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## AN EPIDEMIC OF NOMA.

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THROUGH the kindness of Dr. Jonas E. Reinthaler and Dr. Charles A. Elsberg, respectively attending physician and surgeon to the New York Hebrew Infant Asylum, I had the opportunity of studying an epidemic of noma which occurred in that institution in the spring of 1909. The asylum is a substantial, well-preserved edifice. It was originally a private dwelling, and was later enlarged by the addition of wings. The institution accommodates about 150 children. During the epidemic there were 140 children in the asylum of varying ages, up to six years.

Three cases of noma occurred in the asylum during fourteen years, one in November, 1902, one in February, 1907, and one in February, 1908. All three patients died; in two the treatment was conservative; in the third and last a wide excision was performed by Dr. Elsberg. In the three cases the disease developed in the course of epidemics of measles complicated by ulcerative stomatitis. It is of interest that the three cases, though widely separated in time, occurred in the same ward—a sunny, well-ventilated room.

The epidemic of noma of 1909 complicated an epidemic of measles, which spread in the institution despite careful isolation of all the exposed children. The epidemic of measles was a severe one and complications were frequent. There were 81 cases—of which 13 developed diphtheria, and 24 pneumonia—with a mortality (exclusive of noma) of 4 per cent. Although special attention was paid to the mouths, ulcerative stomatitis occurred in fully 25 per cent. of the children, and it was among these children that most of the cases of noma developed. There were 8 cases of true noma and 3 doubtful ones, to which reference will later be made.

One of the most striking facts about noma is that it has formerly broken out, almost invariably, in overcrowded and ill-regulated hospitals. For example, Saviard and Poupart<sup>1</sup> recorded epidemics of noma in the old Hôtel Dieu in Paris under such circumstances; in the new institution the disease did not develop. There are many similar reports in the literature of the disease. On the other hand,

<sup>1</sup> Trans. Med. Chir. Soc., Edinburgh, 1892-9, xii, 251.

in recent years epidemics have broken out in excellent institutions, as in that reported by Blumer and McParlane<sup>2</sup> and in that of Crandon, Place, and Brown.<sup>3</sup>

The association of noma with the infectious diseases—especially measles and pertussis—is well known. The pronounced tendency for noma to appear in the spring and fall may depend upon the greater frequency of the infectious diseases in those seasons. There is no conclusive proof that the disease is contagious. Mayr<sup>4</sup> believes in its contagiousness; Holt<sup>5</sup> is of the same opinion, as he has seen 5 cases of noma, after whooping cough, develop in the same ward. Of the cases in our epidemic, 2 developed in one ward, 3 appeared in another, and 5 (including the three not proved) developed in a third ward, which was reserved, as far as possible, for all of the cases of stomatitis. A single case developed in the isolation house to which the child, suffering from diphtheria, had been transferred. Two of the wards were on the same floor, the third was on another. Each ward was carefully isolated, had its special nurses, separate food, dishes, etc. The children who developed noma were transferred to the isolation house as soon as the disease appeared. It is often impossible to say when noma is developing, and undoubtedly many children were exposed to the disease when they were presumably in a receptive condition—suffering from measles and ulcerative stomatitis. With these conditions, favorable for the spread of a contagious disease, only a few of the little patients were attacked by noma, and no connection could be demonstrated between the isolated cases.<sup>6</sup>

Noma may appear at any age and among all cases of patients. The large majority of the cases have occurred among poorly nourished children<sup>7</sup> during the first and second dentition, and many apparently developed from ulcers around the teeth. Rilliet and Barthez,<sup>8</sup> in their classic description of the disease, describe noma in infants at the breast. Inasmuch as noma so often follows ulcerative stomatitis, many writers (Eichhorst,<sup>9</sup> Henoch,<sup>10</sup> Guizetti,<sup>11</sup> Seiffert,<sup>12</sup> etc.) consider noma an advanced stage of stomatitis. They point out that at first it is a purely local disease, that the same organisms

<sup>2</sup> AMER. JOUR. MED. SCI., 1901, exxii.

<sup>3</sup> Boston Med. and Surg. Jour., April 15, 1909.

<sup>4</sup> Zeitschr. der Kais.-Kön. Gesellsch. der Aerzte zu Wien, 1852.

<sup>5</sup> Diseases of Infancy and Childhood, 1905, pp. 290, 692.

<sup>6</sup> Schmorl (Zeitschr. f. Thiermed., 1891, p. 375) described an epidemic, among rabbits, of gangrene beginning in the mouth, which was very similar to noma. He showed that it was contagious.

<sup>7</sup> Some of these cases in the literature described as noma in adults correspond very closely to cases of leukemia with terminal gangrenous ulceration in the mouth. Blood examinations were not recorded.

<sup>8</sup> Traité des Malad. des Enfants, 1852, p. 62.

<sup>9</sup> Specielle Patholog. und. Therap.

<sup>10</sup> Trans. Chicago Path. Soc., 1896, i, 252. ¶

<sup>11</sup> Il Policlinico, 1899.

<sup>12</sup> Münch. med. Woch., 1901.

are found in the smears taken from the ulcers of both diseases, and that the transition from the one condition to the other has been observed. It will be shown below that a definite bacteriological picture is found in noma and not in ulcerative stomatitis.

There are usually no constitutional symptoms until the gangrene has begun to spread. The child is usually quiet and languid, but may be very restless and irritable. Often it is profoundly prostrated, but may feel well enough to sit up in bed and play, although the gangrene is spreading over its face. Marked pallor is an early symptom. The pulse soon becomes rapid and small; there is slight or no fever, and generally no pain. Thirst is marked, although the tongue is moist. Diarrhœa is often a serious symptom, but, according to some observers, occurs only when gangrenous material is swallowed.<sup>13</sup> Bronchopneumonia is the most frequent and fatal complication. It is of the aspiration type, and not uncommonly leads to abscess or gangrene of the lung.

Of the physical signs, the ulcer is usually the first lesion observed (Bohn,<sup>14</sup> Eichhorst, Osler,<sup>15</sup> etc.). Billroth, however, describes a nodule in the cheek as the starting point, and Fagge<sup>16</sup> believes the disease begins immediately under the mucous membrane. The necrotic ulcer becomes gangrenous, the adjoining portion of the cheek becomes intensely infiltrated, and the gangrene extends to it and often to the adjacent maxilla. The peculiarly penetrating foul odor from the mouth is at the beginning faint, yet it may be the first sign to call attention to the disease. As the overlying skin becomes involved, it assumes a violaceous hue, later turns black and is covered with vesicles; finally the gangrenous ulcer breaks through. Tourdes<sup>17</sup> describes three stages of the disease: (1) Ulceration of the mucous membrane, œdema of the face, infiltration of the cheek, lasting two or three days; (2) gangrene, lasting five to twelve days; and (3) the period of general infection. Rarely the disease runs a subacute course over several months. Finally, Gierke noted that noma may recur.<sup>18</sup>

In a large number of cases collected from the literature the mortality ranged from 70 to 100 per cent.

Many different kinds of treatment have been recommended.

<sup>13</sup> Several autopsies have shown a gangrenous condition of the gastro-intestinal tract. In 8 cases of noma of the genitalia and of the external ear observed by Gierke (*Jahrb. f. Kinderheilk.*, 1868, p. 65) diarrhœa was present in only one case, and then it was of short duration.

<sup>14</sup> Gerhardt's *Handb. der Kinderk.*, iv.

<sup>15</sup> *Practice of Medicine*, 1905.

<sup>16</sup> *Amer. System of Diseases of Children*.

<sup>17</sup> *Thèse de Strassbourg*, 1848.

<sup>18</sup> In 20 cases he observed three recurrences—one four weeks after the discharge of necrotic tissue, a second case six months after the first attack, the third case after three years. Babes and Zambilovici (*Annal. de l'Institut. de Path. et de Bact. de Bucarest*, 1895, v) refer to several cases.

Some writers advise applications of alcohol or hydrogen peroxide, or potassium chlorate, nitric acid, etc. Others advise cauterization of the ulcer with the actual cautery; still others practise excision of the diseased area. No matter what the treatment employed, only isolated cases have recovered. It is important to make frequent cultures from the necrotic areas, as diphtheria may closely simulate true noma.<sup>19</sup> If there is any doubt as to the diagnosis, antitoxin should be given.

The bacteriology of noma rests on a definite basis since 1899, when Perthes<sup>20</sup> and Seiffert<sup>21</sup> independently described a bacterium or group of bacteria in this disease. Although, up to the present time, Koch's laws have not been fulfilled<sup>22</sup> the disease has not been experimentally reproduced and the bacteria have not been artificially cultivated—the constant presence of the bacteria in noma, and only in this disease, points very strongly to an etiological relationship. Perthes found that noma is due to a fungus-like growth belonging to the streptothrix group. At the border line between the gangrenous ulcer and normal tissue he found a thick branching network of fine fusiform threads—mycelium. From this mycelium single fine rods and spirilla extend into the normal tissue, surround the cells, and cause their death.<sup>23</sup> Krahn believes that the growth described by Perthes consists of two organisms—the spirillum sputigenum and spirochete dentium.<sup>24</sup> The majority of observers agree with Perthes and Seiffert. The same bacteriological picture was described in noma of other parts of the body by Matzenauer.<sup>25</sup> Perthes prepared his specimens for examination by treating the teased tissue or section from the edge of the ulcer—removed post

<sup>19</sup> Hektoen, in the discussion on Bishop and Ryan's paper before the Chicago Pathological Society, pointed out the close clinical correspondence between their cases of noma and cases of gangrene of the skin in which the Klebs-Loeffler bacillus is found. And Loeffler, at a meeting of the Greifswald Medizinische Verein, in 1890, called attention to the similarity between pathological specimens from cases of noma, shown by Grawitz (Deut. med. Woch., 1890), and diphtheria in calves (Kälberdiphtherie) that he had observed.

<sup>20</sup> Arch. f. klin. Chir., 1899, lix.

<sup>21</sup> Münch. med. Woch., 1901.

<sup>22</sup> Hofman and Küster (Münch. med. Woch., 1904, 1907) found abscesses in animals after the bacteria were injected and found the same bacteria in the abscesses. Furthermore, they obtained (impure) anaërobic growths of the organism. Neither of these observations has been subsequently substantiated.

<sup>23</sup> Ranke (Jahrb. f. Kinderheilk., 1888, xxvii) and others have advanced evidence to show that the death of the cells is due to chemical influences.

<sup>24</sup> Miller (Microorganisms of the Human Mouth, 1890) has shown that these two organisms are normal inhabitants of the mouth, in small numbers. As all attempts at their cultivation have failed, he considers them parasites that cannot be separated from their hosts. In all forms of stomatitis, as well as in oral noma, these bacteria are present in enormous numbers in scrapings from the lesions. The fusiform "bacillus" of Vincent is also found on the surface of these ulcers. But it has not been demonstrated that any of these organisms are related to the streptothrix found in the tissues in noma, although some of the terminal filaments of the streptothrix resemble them closely (see Migula's (System der Bacterien, 1900) classification of these organisms).

<sup>25</sup> Archiv. f. Dermat. und Syph., 1902.

mortem—with dilute carbol-fuchsin for twenty-four hours and then briefly washing with alcohol.<sup>26</sup>

The clinical and bacteriological pictures of the cases of noma in our epidemic correspond in good part with the description given above. However, some features of importance in our cases warrant a description of them in some detail; the detail of the spread of gangrene, the appearance of the streptothrix in individual cases,<sup>27</sup> etc., will be omitted. By "conservative" treatment we mean topical applications of peroxide of hydrogen, pure alcohol, and potassium chlorate; by "radical" treatment, thorough cauterization of the ulcer and of adjoining tissue with the actual cautery.

CASE I.—*Measles; ulcerative stomatitis; noma of the vulva; recovery.*

Jennie W., aged two years, was always delicate. Bilateral chronic otitis media. Measles March 9, 1909, complicated by a severe ulcerative stomatitis. The latter cleared up except for one ulcer. This necrotic area became gangrenous in its centre. A specimen removed did not show the streptothrix of noma. On March 17 a grayish membrane was observed covering the vulva and extending over the labia minora and across the perineum to the rectum. Cultures for diphtheria were negative; antitoxin had no effect. The membrane spread, the affected area became necrotic in forty-eight hours, and there was a profuse discharge of a gangrenous odor from the vagina and rectum. A specimen removed from the edge of the ulcer showed the streptothrix of noma. After two weeks, during which period the child was profoundly prostrated, the discharge diminished and the ulcer assumed a healthier appearance. Although there was a considerable loss of tissue, little deformity remained when healing was complete. Treatment was conservative. During convalescence the ulcer in the mouth slowly healed.

CASE II.—*Measles, ulcerative stomatitis; diphtheria of the vulva; oral noma; recovery.*

Marie F., aged two and a half years; was always well and strong. On March 10 measles developed, in the course of which ulcerative stomatitis appeared. March 16, a membrane was first noticed on the vulva similar to that in the first case. Cultures showed Klebs-Loeffler bacilli; the membrane disappeared after antitoxin injections. As the ragged sloughing ulcers about the teeth showed no signs of

<sup>26</sup> Weaver and Tunnieliff (Jour. Infect. Dis., 1907) demonstrated that this streptothrix is decolorized by Gram's method. They obtained the best staining reactions by dropping a 10 per cent. saturated solution of alcoholic gentian violet in 5 per cent. phenol on the section (that had been embedded in paraffin, treated with xylol, followed by absolute alcohol) for five minutes, clearing with aniline oil, washing with xylol, and mounting in balsam. A complete bibliography of noma is given by Weaver and Tunnieliff, Journal of Infectious Diseases, January, 1907.

<sup>27</sup> The streptothrix stained very well in our cases with the simple method of Perthes. I obtained the specimens by removing a small wedge of tissue from the edge of the ulcer, employing small straight scissors and forceps. A tonsillar "punch" may be employed to advantage.

healing, they were cauterized with the actual cautery on March 25. Following this all but one of the ulcers healed. The latter was situated near the right upper canine tooth; a section removed from it showed the streptothrix of noma. Treatment consisted of cauterization every second day. April 8, infiltration of the upper lip; ulcer much larger; superior maxilla exposed; overlying skin bluish. General condition good; slight fever and prostration. After fragments of the necrotic superior maxilla had separated, improvement began. The violaceous hue of the skin disappeared; the infiltration softened; and finally the slough separated from the ulcer. A specimen removed at this time showed numerous spindle-shaped rods extending into normal tissue, but no mycelium. The treatment was conservative from the time the gangrene began to spread.

CASE III.—*Measles; diphtheria; oral noma; recovery.*

Isidor L., aged two years, had been previously well and strong. Measles March 18, complicated by faucial diphtheria. The membrane disappeared a few days after antitoxin injections. About one week later an ulcer appeared about the upper incisors. Despite several cauterizations, it spread until a large piece of necrotic maxilla was exposed. Treatment by cauterization was then stopped. A specimen removed showed the typical streptothrix. The upper lip became exceedingly firm and infiltrated, but the skin remained unchanged. During a period of ten days this condition was stationary; the child was listless and apathetic, he had no fever, pulse was rapid. Then a large fragment of necrotic maxilla became detached and was removed. Thereafter the local and general condition improved. Treatment was conservative after the spread of the ulcer. Little deformity remained after healing was complete.

CASE IV.—*Measles; pneumonia; oral noma; death.*

Doris A., aged three years, was always pale and weakly. Enterocolitis in 1907, with recurrences from time to time. Measles March 8, complicated by a severe pneumonia. On March 17 an ulcer was seen on the mucous membrane of the right cheek. Cultures negative; antitoxin without effect; characteristic odor from the mouth. The cheek became indurated very rapidly, the overlying skin assumed the typical color, the ulcer spread to the vermilion border of the lip. The child died March 21, apparently overcome by toxemia. The treatment was conservative. A specimen was not removed.

CASE V.—*Measles; diphtheria; ulcerative stomatitis; oral noma; death.*

Harry S., always well and strong. Measles March 12; tonsillar diphtheria March 19. The latter yielded to antitoxin injections. A mild form of stomatitis was present. On March 23 a ragged ulcer appeared below the lower central teeth, where there had been no previous lesion. A section showed the streptothrix of noma. Thor-

ough cauterization was practised; the next day the adjoining maxilla was exposed and the submaxillary region was infiltrated. On March 25 an ulcer appeared about the teeth of the upper jaw exactly opposite the gangrenous lesion of the lower—apparently a contact infection. It spread rapidly, and the eyelids and lip became puffy; an offensive discharge issued from the nostrils. The upper lesion spread more rapidly than the lower. Temperature ranged from 100° to 104°; pulse very rapid and small. The gangrenous ulcers finally perforated the skin over the chin and over the upper lip; pus appeared in the diarrhoeal stool; the patient succumbed March 30.

CASE VI.—*Measles; pneumonia; ulcerative stomatitis; diphtheria; oral noma; death.*

Daniel B., aged three years; always ailing and on special diet for a year. Measles March 14; shortly after, a severe ulcerative stomatitis. Pneumonia with moderate prostration; convalescent by March 20. Faucial diphtheria on March 21, yielding to anti-toxin injections. On March 23 an ulcer was first noted on the inner surface of the left cheek; at the same time a faintly gangrenous odor of the breath was observed. A section removed showed the lesion of noma. Although the ulcer was thoroughly cauterized, it spread and the overlying skin became necrotic; perforation occurred two days before death. The latter occurred on April 3 from a septic bronchopneumonia. This patient suffered considerable pain—an exceptional feature in our cases.

CASE VII.—*Measles; ulcerative stomatitis; oral noma; death.*

Eddie A., aged two and a half years; was always strong and well-nourished. Measles appeared March 6, complicated by ulcerative stomatitis of moderate severity. On March 18 an ulcer was first seen in the normal mucous membrane along the frenum linguæ. With daily deep cauterization, this ulcer remained stationary, whereas the ulcers surrounding the teeth healed. A section taken from the sublingual lesion showed the streptothrix of noma; one removed from one of the other ulcers did not. On April 1 the ragged ulcer under the tongue began to spread on the surface and into the depths. It became gangrenous, spread over the whole floor of the mouth, and caused a marked induration in the submaxillary region. On April 4 an ulcer under the upper lip appeared, opposite the lower ulcer. It spread more rapidly than the original lesion. April 7, gangrene of the skin over both ulcers. Death on April 9.

CASE VIII.—*Measles; ulcerative stomatitis; oral noma; death.*

David R., aged two and a half years; always ailing and weakly. Had measles March 17, complicated by mild ulcerative stomatitis. March 22, apparently on the base of one of the ulcers about the lower central incisors there was a large deep ulcer. A specimen showed the streptothrix. The ulcer was frequently cauterized, and did not grow larger until April 4. It then began to spread, so that



by April 7 the chin was swollen and shiny. The next day a contact (?) lesion appeared on the upper gums and spread like the primary ulceration. A specimen removed showed the same pathological picture as that from the lower lesion. The skin of the chin became gangrenous, and soon after, gangrene of the upper lip developed. The patient died April 11; he was not prostrated until twenty-four hours before death.

In the last three cases frequent cauterization was employed after the ulcers had begun to spread, in order to determine its value in this stage of the disease. This radical treatment had no salutary effect on the lesion; if anything, it appeared to hasten the spread of the gangrene.

To these undoubted cases of noma I would add the three cases to which reference has already been made. All three patients had measles, and in two of them ulcerative stomatitis developed. In both the stomatitis cleared up with the exception of one ulcer. In the third case there was a single ulcer from the outset. The ulcer, in each case, was deep, ragged, and necrotic, identical with the ulcer observed in the pregangrenous stage of noma. Specimens taken from the edge of the ulcer showed in each case the streptothrix of Perthes. The ulcers were submitted to frequent and thorough cauterizations, and after a period of two to four weeks they healed without any spread of necrosis and without the development of serious constitutional symptoms.

Among the patients with stomatitis there were several who had very suspicious ulcers. Specimens removed did not show the streptothrix, and none of these patients developed noma.

It will have been noted that for the cauterizations and for the removal of specimens no anesthesia was employed. This was done for the following reasons: In the first place the manipulations may be carried out quite painlessly. In the second place, these children are already much weakened by their disease, and the function of their lungs is impaired by the associated pulmonary affection; in them a general anesthesia must certainly be very dangerous. In not a few of the patients who were operated upon under general anesthesia septic pneumonia followed.

In Cases II, VII, and VIII, the spread of gangrene was delayed about two weeks, in each case, by repeated cauterizations, and I believe that if cauterization had been begun earlier, the spread of noma might have been much longer delayed. It cannot, of course, be proved that the three cases of ulcer identical clinically and histologically with the pregangrenous ulcer of noma were really cases of noma aborted by radical treatment; the findings, however, all point in that direction. It appears to me, from our experience, that the radical treatment is of value only in the pregangrenous stage of noma. We have found the streptothrix in this stage, and hence have concluded that it is unnecessary to wait for the appearance of gan-

grene in order to institute radical treatment. As before stated, actual cauterization is as effectual as excision and is less mutilating.

The close association of noma with ulcerative stomatitis was seen in this epidemic. Ulcerative stomatitis of varying severity was present in 8 of the 11 patients; in some of the cases the ulcers were necrotic, almost gangrenous. Yet in only one (Case VIII) did it seem probable that noma had developed on one of the lesions of ulcerative stomatitis. From the observation of all the cases in this epidemic, and from the microscopic studies, we must conclude that disease of the mouth prepared a favorable soil for the development of noma, but that there was no evidence of a direct etiological connection between stomatitis and noma.

What significance should be attached, in Cases V, VII, and VIII, to the development of gangrenous ulcers—apparently by contact—cannot be determined. Such a path of transmission of the disease would seem probable; it occurred in three of our five fatal cases. In one of these patients the microscopic examination revealed the streptothrix in sections from the second ulcer. I have been unable to find any mention in the literature of second ulcers in noma.<sup>28</sup>

CONCLUSIONS. Noma usually appears in epidemic form; its contagiousness has not been proved. The disease is an entity, and not a later stage of ulcerative stomatitis; the latter offers a good soil for the development of noma. There is regularly present in noma a streptothrix characterized by a thick meshwork of mycelium at the border line between normal and necrotic tissue; fine rods and spirilla extend from mycelium into the adjacent tissues. The constant presence of this streptothrix, to the exclusion of other organisms, indicates that, in all probability, it stands in direct etiological relationship to noma. The streptothrix is present in noma before the disease is fully manifest—in the pregangrenous stage. It is in this stage of the disease that radical treatment is to be practised; after the ulcer spreads, the best results are obtained by conservative measures. General anesthesia should not be employed in any form of treatment because of the pronounced tendency to the development of septic pulmonary disease.

<sup>28</sup> Blood examinations were made in four cases. There was a marked anemia (2,000,000 red cells), with decided poikilocytosis and anisocytosis; no leukocytosis. The blood drop was very watery and was expressed with difficulty. Cells resembling myelocytes were present in the spreads. In three patients Wassermann tests were kindly made by Dr. Kaplan, bacteriologist to the Montefiore Home, with negative results. They were done because it has been suggested that the organism of noma is in the same class as *Treponema pallidum*.

## THE ANTITRYPTIC ACTIVITY OF HUMAN BLOOD SERUM: ITS SIGNIFICANCE AND ITS DIAGNOSTIC VALUE.<sup>1</sup>

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It is not much more than a year ago that Brieger and Trebing announced that a new characteristic of the blood in cases of cancer had been determinend. This new feature consisted in a marked increase in the power of the serum to inhibit the proteolytic activity of solutions of trypsin, and was so constant an accompaniment of cancer as to be present in over 95 per cent. of the cases. Since the publication of their original paper, investigations on this subject have followed each other in rapid succession, so that the literature has come to assume a very goodly volume. As the result of this accumulation of data, it has become increasingly evident that the "antitryptic reaction," as it is called, is not an exclusive characteristic of cancer: it appears under certain other conditions of disease; it marks the change from breast to artificial feeding in infants; it is a striking feature of the onset of labor and the puerperium, as contrasted with pregnancy; in other words, it appears to be a physiological adaptation of widespread significance and value. On the other hand, the fact is not to be gainsaid that the accumulation of evidence has not materially weakened the assumption originally maintained by Brieger and Trebing—the antitryptic reaction is an almost constant accompaniment of cancer, and occurs in a very much smaller proportion of all other diseases. The significance of this association between cancer and this biological change in the character of the serum must be regarded as a matter of some importance, aside from any practical diagnostic application which may attach to it. It is part of the larger problem of the general constitutional influence exercised by the newgrowth upon its host. In a larger view, the physiological value of the reaction, and its general relation to the subject of immunity, is a matter which requires elucidation. In the present paper the subject will be considered from the various points of view which have occupied investigators, and which have been outlined above.

**METHODS.<sup>2</sup>** The methods at present in use for determining the antitryptic value of serum are the fruit of a long process of evolution, the details of which need not here be sketched. There are essentially two methods in common use. The first of these, which was em-

<sup>1</sup> Referat to the American Association for Cancer Research, read at a meeting held in New York City, November 27, 1909.

<sup>2</sup> A more detailed critique of these methods may be found in a paper by the author, *Archives of Internal Medicine*, 1910, p. 109.

ployed by Brieger and Trebing,<sup>3</sup> makes use of plates of coagulated serum as the medium of digestion; on such plates a drop of solution of trypsin within twenty-four hours makes a visible depression or dell. A series of mixtures of the serum under examination, and of a standard solution of trypsin, is prepared, in which a constant quantity of the serum is added to increasing amounts of the ferment. Of each of these mixtures a loopful is transferred to the surface of the plates, which are then incubated at 55° for twenty-four hours. In this manner it is possible to determine in each case just how much of the trypsin solution can be totally inhibited by the standard quantity of serum, and so, to determine the "antitryptic titer" of the serum. The other method, known both as that of Fuld and of Gross,<sup>4</sup> employs a solution of casein as the medium of digestion. The serum in constant, and the trypsin solution in ascending, quantities, are added to a series of test-tubes containing equal amounts of casein in solution. At the end of two hours of incubation, the undigested casein is precipitated in all of the tubes by acidification; note is made of the lowest amount of trypsin which produces complete digestion, and this is taken to indicate the limit of the inhibitive activity of the serum. The results in both methods are expressed in figures, which denote the number of tenths of a cubic centimeter of trypsin inhibited. Through a preliminary determination of the inhibitory limits of normal serum it becomes possible to determine that certain serums have greatly diminished or greatly increased inhibitory power.

As regards the purely technical details of these methods, it may be said that both of them suffer from rather serious defects. The serum-plate method is open to the same objection which has been made to Mette's method of measuring the peptic activity of the gastric juice by means of the quantitative measurement of the amount of egg albumen which it is capable of digesting. Both egg albumens and the coagulated serums of different animals differ very considerably among themselves in digestibility, so that there is not the required constant basis of comparison (Klineberger and Scholz<sup>5</sup>). Furthermore, the visual appreciation of a minute depression on the surface of a serum plate is a very difficult and inexact procedure. When to these sources of error is added the fact that incubation is necessarily carried out at 55°—certainly far from the optimum for trypsin—and that bacterial contamination is a possible, though not a frequent, element of confusion, it may be understood that the method yields results only approximately accurate. The casein method is certainly far simpler and easier to manipulate. In addition to this, it has the added advantages of greater accuracy in the mixture of reagents, a normal temperature of incubation, and a period of experiment so short as to exclude bac-

<sup>3</sup> Berl. klin. Woch., 1908, p. 1041.

<sup>5</sup> Deut. Archiv f. klin. Med., 1908, p. 319.

<sup>4</sup> Archiv f. exp. Path., 1907, p. 137.

terial contamination; furthermore, the "end-points" of the readings are fairly sharp and accurate. Brieger<sup>6</sup> has objected, with regard to this method, that the classification of serums is more or less inexact; that the results are inconstant; and that the acid may produce a soluble acid albumin, and so obscure the "end-point" of the series of readings. None of these objections, however, is valid in fact; they are all purely theoretical. Numerous other objections have been made to the methods, the most important being that recently advanced by Marcus,<sup>7</sup> who was one of its originators. He states, as is well known to be the fact, that only a portion of the trypsin goes into solution, and hence maintains that there must be a considerable degree of variation in the strength of solutions presumed to be equal. He proposes to obviate this very serious difficulty by means of the use of glycerin extracts of the trypsin, which preserve their strength unaltered for considerable periods of time, and hence may be kept as standard stock solutions. Although apparently valid, this objection does not withstand the test of experiment. As shown by Dr. Feldstein and myself, the strength of a series of solutions of trypsin, made up independently with equal amounts of the ferment and salt solution, is astonishingly constant, and there is no need of the modification suggested by Marcus. The insoluble material is apparently evenly distributed as an inert impurity in the commercial tryptins.

The most serious objection which can be made to the method concerns the notation of results. This is apparently very simple. The results are stated in units, which represent the amounts of trypsin inhibited, in tenths of a cubic centimeter of the standard solution used. This mode of representing the results depends on the assumption that the amount of antitrypsin contained by serums is directly proportional to the quantity of trypsin which they are capable of inhibiting. In other words, the method presupposes that a serum of the titer 0.6 is twice as strong as one of 0.3. Neither the method of Brieger nor of Bergmann permits of an experimental tests of this hypothesis, but determinations made with the viscosimeter demonstrate that these relationships are distinctly not so simple as demanded by the theory. If an arithmetical series of solutions of trypsin be prepared, and the necessary inhibitory amount of serum determined for each member of the series, it is found that the quantitative intervals in the higher determination become increasingly larger. Consequently, the proportion indicated by the figures obtained by the serum or casein methods is entirely incorrect. Nevertheless, the relative antitryptic strength of the serums is correct, at least from a quantitative standpoint, and it is fair to accept the grouping of serums obtained by these methods as approximately accurate.

<sup>6</sup> Berl. klin. Woch., 1908, 1415, in report of discussion.

<sup>7</sup> Ibid., 1909, p. 156.

The viscosity method<sup>8</sup> previously referred to depends on the fact that the amount of digestion produced by trypsin in gelatin may be measured by determining the alteration in the viscosity of the latter medium. The effect of serum in controlling the activity of the trypsin is, of course, very simply determined. The method offers certain very distinct advantages over those previously employed. Whereas, by the serum or casein methods, it is possible to make only one determination, namely, either the point of complete inhibition or of total digestion, the viscosimeter determines the degree of inhibition at any moment of time. The method, therefore, substitutes the use of a single mixture for that of a series, which is a very considerable gain in simplicity of technique. Moreover, the method is incomparably more flexible than those previously used, and permits of the determination of a large number of factors otherwise inaccessible to investigation.

The results obtained by the use of the two earlier methods have been strikingly concordant. Indeed, in comparing the findings yielded in a series of cases by both the serum and the casein methods, I found that the data were practically interchangeable. Brieger originally asserted that about 95 per cent. of the cases of cancer evinced a marked increase in the antitryptic value of their serum.<sup>9</sup> He subsequently found that in a large number of other conditions, including both acute infections and chronic wasting diseases, the same phenomenon could be observed, and he consequently concluded that all diseases associated with intense destruction of body protein produced this characteristic alteration in the plasma of the blood. Hence, although he continued to affirm the diagnostic value of the method in all cases of undetermined newgrowth, he reached the conclusion that in general all conditions of "cachexia"—using that term in the broad metabolic sense of wasting disease, either acute or chronic—were competent to produce it. Further investigation has, in general, given ample confirmation to these conclusions, if the term cachexia is interpreted in the peculiar sense in which it was used by Brieger. All observers are agreed that the great majority of cases of cancer give evidence of increased antitryptic value in the serum. In some series the percentage of positive results in cases of cancer ranges as high as 95 per cent.; in others as low as 70 per cent. It is, however, very frequently found in the acute infections, such as pneumonia, typhoid fever, sepsis, and polyarticular rheumatism; in chronic infections, notably tuberculosis; in diabetes and severe anemias; and in Graves' disease almost constantly. These data amply demonstrate that the change in the serum is not to be regarded as a characteristic biological response to the presence of newgrowths. They indicate that it is an evidence of pathological derangement of much wider

<sup>8</sup> Since the presentation of this paper, a preliminary report on the viscosity method has appeared, Feldstein and Weil, *Proc. Soc. Exp. Biol. and Medicine*, February, 1910.

<sup>9</sup> *Berl. Klin. Woch.*, 1908, pp. 1349 and 2260.

distribution. Furthermore, it seems misleading to consider the reaction as characteristic of conditions of cachexia, in view of the fact that this term must be extended so as to include a large number of conditions which can by no possibility be classified as cachectic. The general condition of nutrition of patients whose serum yields the reaction is frequently excellent, and could never be understood as cachectic. The theory of causation involved in the term "Kachexie Reaktion" will be subsequently discussed, but the term itself should certainly be allowed to fall into disuse.

Not only under pathological conditions, however, does this reaction occur. It has been found to accompany and characterize certain processes which may be called physiological, although they denote a certain alteration in the normal course of metabolism. Its occurrence in the blood of infants has been investigated, and it has been found that such infants as are being nourished at the breast never display an increased antitryptic content of the blood (Reuss<sup>10</sup>). On the other hand, with the inauguration of artificial feeding, the reaction at once becomes prominent. In pregnancy it has been found that no antitryptic reaction occurs, but with the onset of labor it makes its appearance, and persists through the puerperium (Becker<sup>11</sup>).

It is evident that these findings may be discussed either from the standpoint of their diagnostic value, or as a biological phenomenon of purely theoretical interest. Diagnostically, the opinion of the various authors who have worked upon this problem is strikingly in accord. As a general diagnostic method, the increase in the antitryptic index occurs in too many conditions to have the value of a specific symptom. On the other hand, the absence of the antitryptic reaction in the blood may be taken generally as arguing against the existence of cancer. In the presence of a neoplasm of doubtful character, a positive reaction, in the absence of complicating conditions, notably tuberculosis, argues with a strong degree of probability in favor of the diagnosis of malignancy (Roche,<sup>12</sup> Hort,<sup>13</sup> Braunstein,<sup>14</sup> Bayly<sup>15</sup>).

The method has apparently stood the test of clinical experience, and has proved to be of distinct value when applied rigidly within the prescribed limits. As regards other conditions, Meyer<sup>16</sup> asserts that the reaction occurs with such regularity in cases of Graves' disease, that it may be relied upon in the diagnosis of the numerous obscure and abortive forms of the disease known as *formes frustes*. It has been claimed by Wiens<sup>17</sup> that the strength of the reaction has

<sup>10</sup> Wiener klin. Woch., 1909, p. 1171.

<sup>12</sup> Archives of Internal Medicine, 1909, p. 249.

<sup>14</sup> Deut. med. Woch., 1909, p. 573.

<sup>15</sup> Brit. Med. Jour., 1909, p. 1220. (Bayly measured digestion by electroconductivity.)

<sup>16</sup> Berl. klin. Woch., 1909, p. 1064.

<sup>17</sup> Deut. Archiv f. klin. Med., 1909, p. 62.

<sup>11</sup> Münch. med. Woch., 1909, p. 1363.

<sup>13</sup> Brit. Med. Jour., 1909, p. 966.

marked prognostic value in the acute infections, but this view is certainly erroneous.

Looked at as a biological phenomenon, the reaction suggests many problems, and has given rise to a considerable amount of research. The chemical nature of the antitrypsin, its character as a specific "immune body," its relationship to artificially produced antitrypsin, and the causes of its production, are subjects which demand elucidation, if the physiological significance and the pathological import of the reaction are to find an explanation.

The chemical basis of the antitryptic reaction has not been satisfactorily determined. It was originally asserted by Glaessner<sup>18</sup> that the antitrypsin was associated with the euglobulin fraction of the serum, which is that part of the serum globulins least soluble in water, and roughly corresponds to the fraction which comes down in dialyzing or on adding acetic acid to the diluted serum (Hedin<sup>19</sup>). Cathcart,<sup>20</sup> on the other hand, asserts that the globulins do not possess antitryptic action, but that this is characteristic of the albumin fraction, that is, the fraction precipitated between half and full saturation with ammonium sulphate. Schwarz<sup>21</sup> has reached the conclusion that the antitryptic fraction of the serum exists in the form of a lipid. He found that he could inactivate antitryptic serums by washing out the lipoids with ether. Such serums could be reactivated by the addition of lecithin. Lecithin in salt solution emulsion, if added to serum, exercised considerable tryptic inhibition; if the mixtures were kept at 65° for one hour, this inhibitory activity was markedly enhanced, indicating that the inhibitory substance is a lipid-albumin compound. Furthermore, he found by analysis that increase in the antitryptic titer of a serum was constantly associated with an increase in the amount of ether-soluble substances which it contained. These conclusions substantiate the earlier findings of Pribram. Interesting as are these data, they fail to support the contention that antitrypsin is a lipid substance. It is well known, for example, that lipoids are essential to the activation of cobra venom in the production of hemolysis; nevertheless, it would be erroneous to consider the lipid substance as the active hemolysin. Lipoids have been shown (Bang<sup>22</sup>) to play an analogous auxiliary role in many processes of immunity, while the essential factor, the active agent, is a protein. It is conservative to maintain this position with reference to antitrypsin, admitting meanwhile the possible importance of lipoids as subsidiary factors.

Is the so-called antitryptic action of the serum dependent on the presence of an "immune body," or is it an accidental property of the serum? This question is really of fundamental importance, though not at all easy to answer. It was found by Vernon<sup>23</sup> that

<sup>18</sup> Hofmeister's Beiträge, 1903, iv, 79.

<sup>19</sup> Ibid., 1904, xxxi, 496.

<sup>20</sup> Ergebnisse d. Physiologie, 1909, p. 463.

<sup>19</sup> Jour. Physiol., 1903, p. 193.

<sup>21</sup> Wien. klin. Woch., 1909, p. 1151.

<sup>22</sup> Jour. Physiol., 1904, p. 346.



egg albumin in solution inhibits the digestive action of trypsin very actively. But it is a still more striking fact that charcoal has been shown to act as an antitryptic agent, in a manner very similar to serum. The amount of inhibition is proportional to the quantity of charcoal, to the time of interaction, and to the temperature, just as it is in the case of serum. In fact, "the action of charcoal was found to agree with that of the tryptic antibody in all respects tried, and therefore the neutralizing effect, in all probability, is brought about in the same way in both cases" (Hedin<sup>24</sup>). It is perfectly apparent that neither egg albumen nor charcoal can in reality contain a true antitrypsin, and that, therefore, the effect observed is simply an accidental phenomenon. It is true of all human serums that they very notably inhibit the hemolytic effect of saponin; it would, however, be entirely unjustifiable to argue from this fact to the existence of an "antisaponin." These theoretical objections to the assumption of an "antitrypsin" in the serum have, unfortunately, not received recognition in the recent literature. On the other hand, it must be admitted that certain observations argue strongly in favor of a true antitrypsin, as against a general property of serum albumin, in the interpretation of tryptic inhibition. Chief among these is the alleged specificity of the antitryptic action. Specificity is, as is well understood, one of the most striking characteristics of all forms of antibody, and its absence may well be interpreted as a powerful argument in the negative. Eisner,<sup>25</sup> as the result of a series of tests made with the same serums against rennet, pepsin, emulsin, and cobra lipase, arrived at the conclusion that serum does not exhibit the properties of a general ferment inhibitor, but that it possesses a special and characteristic affinity for trypsin. This observation seems to indicate the existence of a specific antibody, a true antitrypsin. Glaessner has also, on insufficient evidence (Cathcart), asserted that the antitrypsin of serum is most active against the trypsin of the same species, and is somewhat specific even for various animal trypsins. The facts do not, however, appear to bear out these contentions. It has been possible in our laboratory, by means of the viscosimeter, to demonstrate that all human serums inhibit papain, which is a vegetable proteolytic ferment, in a constant ratio to the degree with which they inhibit trypsin. It seems, therefore, impossible to accept the specificity of the antitrypsin of the serum. The antitryptic function is exercised by an albuminous substance, thermolabile, indeed, like the true antibodies, but differing essentially from these in the lack of specificity. In view of this fact, and of certain other differences, the argument (Meyer<sup>26</sup>) in favor of a true antibody as the basis of this function of the serum loses very materially in credibility.

<sup>24</sup> Biochemical Journal, 1906, p. 484.

<sup>25</sup> Ztschr. f. Immunitätsforschung, 1909, ii, 650.

<sup>26</sup> Berl. klin. Woch., 1909, p. 2139.

This conclusion makes it very much simpler to dispose of the much debated problem as to the identity of the normal antitrypsin of the serum with that produced artificially in animals by the injection of trypsin. All antiferments hitherto produced by this method have been found to be characteristically specific. Thus, by the injection of rennet, Morgenroth<sup>27</sup> succeeded in producing an anti-rennin which powerfully inhibited the action of the injected ferment, but had no influence on vegetable rennet. The entire subject of antiferments is, however, in such a condition of confusion that it is almost impossible to draw any very definite conclusions. Achalme<sup>28</sup> produced an active antitrypsin by the injection of trypsin, but Landsteiner failed to reproduce this result. In our own laboratory, the injection of trypsin into guinea-pigs has been uniformly without effect. The most striking experiments are those recently reported from the Pasteur Institute on the result of the injection of pepsin and of papain. It has been shown by Cantacuzène and Jonescu<sup>29</sup> that when rabbits are immunized to pepsin by the injection of increasing doses, the serum responds by the production of an antibody capable of fixing complement, but possesses no increased antiferment action. Similarly, Pozerski<sup>30</sup> has shown that the serum of animals immunized to papain contains a specific precipitin, and an antibody which fixes complement in a characteristic fashion; but this very immunized serum is just as easily digested by the ferment as is normal serum. The natural antitrypsin, so-called, differs, therefore, in many important particulars from the antibody artificially produced by the injection of ferments into animals, and this fact constitutes an additional argument for regarding it as something essentially different from a true antibody.

The conception of antitrypsin as an antibody has, however, dominated practically all the theories which have hitherto been advanced in the attempt to explain it. In spite of the fact that it cannot properly be so regarded, these theories do not necessarily forfeit their validity. It is perfectly reasonable to assume that the serum may respond to a given stimulus by means of a protective mechanism which does not answer to the criteria characteristic of antibodies and amboceptors. It has generally, and very naturally, been assumed that the presence of antitrypsin in the serum is evidence of an effort on the part of the organism to protect itself against self-digestion. If this be the case, then a tryptic ferment should, theoretically, be present in the serum, and this has actually been demonstrated to be the fact by Hedin and by Delezenne;<sup>31</sup> it is, therefore, an important matter to determine its source of supply.

<sup>27</sup> *Centralbl. f. Bakteriologie*, 1899, p. 349.

<sup>28</sup> *Annales de l'Institut Pasteur*, 1901, xv, 736.

<sup>29</sup> *Compt.-rend., de la Soc. de Biol.* 1909, p. 53.

<sup>30</sup> *Annales de l'Institut Pasteur*, 1909, p. 205.

<sup>31</sup> *Compt.-rend. de la Soc. de Biol.*, 1903, iv, 132.

There are four of such sources theoretically conceivable at present, namely, the pancreas, the leukocytes, the organs, and the new-growths. Each of these has had, and has, its champions, and each requires consideration. The pancreas, as a source of supply of trypsin, is a very obvious suggestion. Ambard<sup>32</sup> suggests that the antitryptic reaction is so marked in cases of gastric carcinoma, because this condition is associated with compensatory overactivity of the pancreas. There is, however, no evidence that the pancreatic trypsin is absorbed from the intestine, and circulates in the serum. Moreover, the explanation fails to explain the increase in Graves' disease, or the acute infections. The polynuclear leukocytes, as is well known, contain an active proteolytic ferment in most respects identical with trypsin. It has been urged that the constant disintegration of leukocytes must necessarily free a considerable amount of this ferment in the serum, and Hedin is of the opinion that the tryptic ferment which he succeeded in isolating from the serum actually represents the remnant of the intraleukocytic ferment. The view that the antitryptic reaction of serum is the manifestation of a response to the excessive disintegration of leukocytes has been urged and defended by Jochmann,<sup>33</sup> Wiens,<sup>34</sup> Weins and Schlecht,<sup>35</sup> Bittorf,<sup>36</sup> Landois,<sup>37</sup> and many others. As a result of the study of a large number of pathological conditions in which the differential leukocyte curve has been carefully plotted, and the antitryptic strength of the serum also has been repeatedly determined, it appears that there are certain definite relationships between these two factors. It has been quite satisfactorily demonstrated that with the onset of an infection the antitryptic index of the serum falls, and that with the progress of the infection it gradually rises again to the level of the normal, and then passes well beyond this to a highly increased index (Landois). Wiens, and Wiens and Schlecht, have shown that these fluctuations in the antitryptic index are accurately foreshadowed by variations in the leukocyte count, but only in so far as the polynuclear leukocytes determine these variations. The mononuclear cells do not play any role in influencing the index, and it is, therefore, of importance in the understanding of the interrelationship of these phenomena that the differential count should invariably be made. The explanation of these relationships is based on the well-known fact of the trypsin content of the polynuclear cells. With the onset of acute infections there is an immediate and rapid increase in the number of circulating polynuclear leukocytes. The inevitable destruction of a certain

<sup>32</sup> Sem. m'ed., 1908, p. 532.

<sup>33</sup> Münch. med. Woch., 1908, iv, 728; Hofmeister's Beiträge, 1908, p. 449.

<sup>34</sup> Deut. Arch. f. klin. Med., 1907, p. 456; Münch. med. Woch., 1907, p. 2637; Centralbl. f. Inn. Med., 1908, p. 773.

<sup>35</sup> Deut. Archiv f. klin. Med., 1909, p. 44.

<sup>36</sup> Ibid., 1907, xci, p. 212.

<sup>37</sup> Berl. klin. Woch., 1909, p. 440.

proportion of these cells frees an excessive amount of trypsin, which at once neutralizes all the available antitrypsin in the serum. Consequently, the antitryptic index falls well below normal, and may even disappear. This is the so-called negative phase of the antitryptic curve. The excess of trypsin in the blood, however, stimulates the production, or the mobilization, of fresh quantities of antitrypsin, which, in accordance with Ehrlich's interpretation of Weigert's laws of regeneration, are well in excess of the amount of trypsin to be neutralized. Consequently, there is a rapid rise in the antitryptic index. This is the so-called positive phase of the curve. A regulating mechanism of some kind tends, however, to keep the amount of antitrypsin in circulation only a little in excess of the trypsin, and this gives the value of the normal index. Fluctuations of this character, in which the leukocyte count and the curve of the antitryptic index pursue a parallel course, constitute a very striking feature of all infectious conditions. Wiens went so far as to assert that in such conditions a constantly increased antitryptic index was an omen of ill import, and augured the paralysis of the mechanism of defence, specifically the polynuclear leukocytes. Thaller<sup>38</sup> reached similar conclusions with reference to puerperal sepsis. In this belief they were unquestionably in error, inasmuch as the index is dependent quite as much on the amount of antitrypsin liberated by the body as on the leukocytes which represent the reaction to the disease. Indeed, the majority of acute infections, whether the body is in the ascendant or not, are associated with an increase in the antitryptic index. In addition to these clinical observations, there is ample experimental evidence (Miller<sup>39</sup>) that the injection of leukocytes, or of leukocyte extracts, into animals is followed, after a preliminary fall, by a marked rise in the antitryptic index. It may be seen from the preceding analysis that cases of myelogenous leukemia would not necessarily be associated with any notable variation in the antitryptic index, inasmuch as the regulatory mechanism maintains the index at its constant normal level. Joehmann, however, asserts that sudden myelocyte crises may so flood the blood with trypsin that the serum actually assumes digestive power, in place of its normal inhibitory function.

The preceding theory, interesting as it is, does not fully explain the phenomena. There are many conditions, such as diabetes, Graves' disease, and so forth, in which there is no increased production of leukocytes, yet the antitryptic index is constantly increased. If the leukocyte curve be admitted to afford a satisfactory explanation of the index in infectious conditions, there still remains a considerable number of conditions in which some other explanation must be discovered. In addition to the pancreas and the polynuclear leukocytes, there is another possible source of trypsin in the

<sup>38</sup> Berl. klin. Woch., 1909, p. 850.

<sup>39</sup> Zentralbl. f. Chir., 1909, p. 75.

body, namely, the cells of the tissues. It has now been abundantly shown that many, if not all, of the tissues contain proteolytic ferments, which are competent to break up these tissues outside of the body into a much simpler group of compounds. This process is known as autolysis, and the ferments in question are called autolytic ferments. Although they are actively proteolytic, they appear to differ in certain particulars from true trypsin. Thus, the end-products indicate that an ereptic ferment is almost certainly at work (Vernon<sup>40</sup>). Furthermore, it has been asserted by Jacoby<sup>41</sup> that these ferments are adapted specifically to the proteolysis only of the organs in which they occur, a characteristic which, *if well founded* (Beebe),<sup>42</sup> would sharply differentiate them from true trypsin. In spite of these objections, there are certain facts which indicate their possible relationship with the antitryptic phenomenon of the serum. In the first place, it is known that the injection of tissue other than the pancreas may induce a rise in the antitryptic index. Further, serum exercises an anti-autolytic (Baer and Loeb<sup>43</sup>), just as it does an antitryptic, power. Finally, it has been shown by Shaffer and Buxton,<sup>44</sup> and others, that glycerin extracts of the various organs, including the muscles, are capable of displaying marked proteolytic powers, when tested, for example, upon milk agar plates. The difficulty in all observations of this kind consists in excluding the leukocytes themselves. If it must be admitted that the conditions of experimentation have not yet permitted a final decision as to the character of the ferments contained in the organs, the fact still remains that the tissues do contain a proteolytic ferment, probably very similar to trypsin. In view of this fact, the theory has been advanced that the destruction of body protein from any cause would tend to free the proteolytic ferments contained in the cells, and that the somatic reaction would liberate an excess of antitrypsin in the serum. This theory, it will be seen, is simply an expansion of the leukocyte theory, inasmuch as the leukocytes may be considered as a type of cell distinguished by their increased content of proteolytic ferments. There can, indeed, be no question that it offers an explanation for the increased index in a large number of diseases for which the leukocyte theory is entirely inadequate, such as the marasmus of infants (Lust<sup>45</sup>). This includes not only conditions such as Graves' disease, diabetes, and chronic tuberculosis, but certain acute infections, such as typhoid fever, not associated with leukocytosis. There is, however, one very weak point in this theory, in spite of the fact that it apparently harmonizes with clinical conditions, and this is the unwarranted assumption that heightened protein metabolism is necessarily associated with the liberation

<sup>40</sup> Intracellular Enzymes, 1909.

<sup>42</sup> Boston Med. and Surg. Jour., 1907.

<sup>43</sup> Arch. f. exp. Path., 1905, p. 1; 1906, p. 63.

<sup>44</sup> Jour. Med. Research, 1905.

<sup>41</sup> Ztschr. f. Physiol. Chem., 1901, vol. xxxiii.

<sup>45</sup> Deut. med. Woch., 1909, p. 1901.

of intracellular ferments. The advocates of the theory have devoted a great deal of effort to the support of this assumption. It has been asserted (Fürst) that starvation, with its accompanying cellular destruction, raises the index, but this again has been denied (Meyer). The effect of cellular poisons, such as pilocarpin, phosphorus, and potassium cyanide, has been tested, but without the expected result in raising the index. The kidneys have been tied off, and allowed to necrose *in situ*, but in spite of the presumptive absorption of the cellular constituents including ferments, no rise in the antitryptic index was observed. It must be admitted, therefore, that experimental data fail to give any support to this theory.

The increase of the index in cancer is attributed to the same cause, namely, the liberation of the intracellular ferments, which are well known to be very active in cancerous growths (Bamberg<sup>46</sup>). With the frequent tendency to necrosis in tumors, even if only in microscopic areas, there would seem to be abundant opportunity for the absorption of ferments. But here, again, the absence of evidence that such a process actually does occur is a fundamental flaw in the theory.

To sum up, the origin of the hypothetical trypsin which is supposed to act as a stimulant for the production of antitrypsin, or, technically speaking, as antigen, is as yet undetermined. It may, conceivably, arise in the pancreas, or in the leukocytes, or in the tissue cells, or in the newgrowths, or in each one of these, under varying circumstances, but actual evidence that it does so arise is at the present time an absolute necessity for the establishment of the theory. The very first essential is to determine whether or not the trypsin, or proteolytic ferment of the blood is increased, in accordance with the assumption of the hypothesis, in the conditions which give rise to an increase in the antitryptic index. At the present time, no method seems to be available for this purpose.

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## THE WASSERMANN AND NOGUCHI COMPLEMENT-FIXATION TEST IN LEPROSY.<sup>1</sup>

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OF NEW YORK.

THE first to obtain a positive Wassermann reaction in a case of leprosy was Eitner<sup>2</sup> in 1906. A similar report was made by Weichsel-

<sup>45</sup> Berl. klin. Woch., 1903, pp. 1396 and 1673.

<sup>1</sup> Read at a meeting of the Medical Society, of the State of New York, January 24, 1910.

<sup>2</sup> Ueber den Nachweis von Antikörpern im Serum eines Leprakranken mittels Komplementablenkung, Wien, klin. Woch., 1906, No. 15, p. 1555.

mann and Meier<sup>3</sup> nearly two years later. Since then it has been found by a number of observers that leprosy quite frequently gives a positive reaction. In testing 26 advanced cases of the disease, Slatineanu and Danielopolu<sup>4</sup> found 20 strongly positive, 4 moderately positive, and 2 weakly positive reactions. Jundell, Almkvist, and Sandman,<sup>5</sup> in a series of 26 cases obtained 4 strong and 4 moderately positive reactions. In 2 cases the result was unsatisfactory, while in the remaining 16 cases the reaction was negative. Of the positive cases, 5 were of the tubercular and 3 of the maculo-anesthetic type. From this Sandman concludes that the occurrence of the reaction does not depend upon the type of the disease, whether tubercular or anesthetic. Meier<sup>6</sup> on the other hand in a series of 28 cases, found positive reactions only in the tubercular type of leprosy. All of the anesthetic cases gave negative reactions. The number of cases of each type was unfortunately not stated. Similar results were obtained by Bruck and Gessner<sup>7</sup> who found positive reactions in 5 out of 7 tubercular cases and negative reactions in 3 anesthetic cases. Positive reactions have also been obtained by Gaucher and Abrami<sup>8</sup> in 8 cases and by Frugoni and Pisani<sup>9</sup> in 9 out of 11 cases of leprosy, the type of the disease, however, not being stated.

Eitner<sup>10</sup> was also the first to obtain complement-fixation in leprosy, using an extract of leprous tissue as antigen. Similar results were later reported by Slatineanu and Danielopolu,<sup>11</sup> Gaucher and Abrami Sugai,<sup>12</sup> Pasini,<sup>13</sup> and by Frugoni and Pisani. It was also found by Slatineanu and Danielopolu<sup>14</sup> that complement could be fixed by leprous serum employing tuberculin as antigen. Complement-fixation in leprosy was also obtained by Frugoni and Pisani by using tuberculin, tubercle bacilli, and extracts of sarcoma and carcinoma as antigen.

It has been my privilege during the past six months to have em-

<sup>3</sup> Wassermannsche Reaktion in einem Falle von Lepra, Deut. med. Woch., 1908, No. 31, p. 1340.

<sup>4</sup> Réaction de fixation avec le sérum et le liquide céphalo-rachidien des malades atteints de lèpre en présence de l'antigène syphilitique. Séances et mém. d. l. Soc. d. biol., 1908, xi, p. 347.

<sup>5</sup> Wassermann's Syphilisreaktion bei Lepra, Zentralbl. f. innere Med., 1908, No. 48, p. 1181.

<sup>6</sup> Zur Technik und klinischen Bedeutung der Wassermannschen Reaktion., Wien. klin. Woch., 1908, No. 51, p. 1765.

<sup>7</sup> Ueber Serumuntersuchungen bei Lepra, Berl. klin. Woch., 1909, No. 13, p. 589.

<sup>8</sup> Le séro-diagnostic des formes atypiques de la lèpre, 1909, viii, p. 152.

<sup>9</sup> Vielfache Bindungseigenschaften des Komplements einiger Sera (Leprakranken) und ihre Bedeutung. Berl. klin. Woch., 1909, No. 33, p. 1530.

<sup>10</sup> Zur Frage der Anwendung der Komplementbindungsreaktion auf Lepra, Wien. klin. Woch., 1908, No. 20, p. 729.

<sup>11</sup> Sur la présence d'anticorps spécifiques dans le sérum des malades atteints de lèpre, Séances et mém. d. l. Soc. de biol., 1908, xi, p. 309.

<sup>12</sup> Zur klinisch-diagnostischen Verwertung der Komplementbindungs methode bei Lepra. Archiv. f. Dermatol. u. Syph., 1909, p. 313.

<sup>13</sup> Sulla reazione della deviazione del complemento nella lepra. Reviewed in Giorn. Ital. d. Malatt. Vener. e d. pelle, 1909, No. 111.

<sup>14</sup> Réaction de fixation dans la lèpre en employant la tuberculine comme antigène, Séances et mém. d. l. Sec. de Biol., 1908, lxx, p. 530.

ployed the Wassermann reaction in 60 cases of leprosy. Fifteen of these cases were seen in various clinics and hospitals in New York City. The remaining forty-five were seen during a recent visit to the Leper Home in Louisiana, an institution under the direction of Dr. Isadore Dyer of New Orleans. All of these 15 cases with one exception were tested by both the regular Wassermann and the Noguchi methods, the results in all cases being identical. The cases in Louisiana were tested alone by the more convenient method of Noguchi, owing to lack of time at my disposal. The technique used was the same as that described in some of my previous communications<sup>15</sup> and will be here omitted for the sake of brevity. It may, however be remarked that the antigen used in the Wassermann test was an alcoholic extract of syphilitic liver. The antigen used in the Noguchi<sup>16</sup> test consisted of acetone insoluble lipoids. The patient's serum in the Noguchi method was used in active condition. All of the cases examined were undoubted lepers, many of them having been under observation for years. No history of syphilis was obtainable in any case. Certainly no lesions were seen in any patient that could have been regarded as syphilitic.

To summarize the results, of the 38 cases of the tubercular and mixed type, the reaction was negative in 7, weakly positive in 3, positive in 21, and strongly positive in 7 cases. Of the 22 maculo-anesthetic and purely anesthetic cases, the reaction was negative in 19, strongly positive in 1, and positive in 2 cases.

It may be of interest to add that beside the 15 cases of leprosy examined in New York, I have also seen or personally known during the past six months, of 7 other cases (3 of Dr. J. McF. Winfield, and one each of Drs. Wm. B. Trimble, M. B. Parounagian, F. M. Dearborn, and G. H. Fox). It will doubtless seem surprising to some that there should have been so many cases of leprosy in New York City during such a short space of time.

CASES OF TUBERCULAR AND MIXED TYPE WITH POSITIVE REACTION.<sup>17</sup> CASE I.—Patient of Dr. S. Dana Hubbard, service of Dr. Jackson, Vanderbilt Clinic. I. W., West Indian negress, aged thirty-three years. Advanced case of tubercular type. Duration of disease two years. Reaction: strongly positive.

CASE II.—Patient of Dr. G. H. Fox, New York Skin and Cancer Hospital. S.V., man, aged forty years, born in Russia. Active fairly advanced case of mixed type. Duration, two years. Reaction: Strongly positive.

<sup>15</sup> The Principles and Technique of the Wassermann Reaction and its Modifications. *Med. Record*, 1909, p. 421; a Comparison of the Wassermann and Noguchi Complement Fixation Tests, *Jour. Cutan. Dis.*, 1909, p. 338; The Wassermann Reaction (Noguchi Modification) in Pellagra, *New York Med. Jour.*, 1909, p. 1206.

<sup>16</sup> On Non-specific Complement-fixation, *Proceed. Soc. Exper. Biol. and Med.*, December, 1909.

<sup>17</sup> Cases not designated by the name of physician and name of clinic where treated, were all seen at the Louisiana Leper Home in the service of Dr. Isadore Dyer.



CASE III.—Patient of Dr. G. H. Fox, New York Skin and Cancer Hospital. P. N., man, aged forty-two years, Italian, Armenian. Advanced case of mixed type. Duration said to be two years. Reaction: Strongly positive.

CASE IV.—Patient of Dr. G. H. Fox, New York Skin and Cancer Hospital. S. V., man, aged twenty-seven years, Italian. Very marked active case of tubercular type. Duration, three years. Reaction: Positive.

CASE V.—Patient of Dr. L. Duncan Bulkley, New York Skin and Cancer Hospital. R. R., Russian woman, aged sixty years. Advanced case of mixed type. Duration, ten years. Reaction: Positive.

CASE VI.—Patient of Dr. J. McF. Winfield, Kings County Hospital. C. W., negro, aged twenty-six years, born in United States. Mixed type of moderate severity, of eight years' duration. Reaction: Positive.

CASE VII.—Patient of Dr. J. McF. Winfield, Kings County Hospital. L. M., man, aged about fifty years, Russian. Advanced case of mixed type. Duration, about twenty years. Reaction: Positive.

CASE VIII.—Patient of Dr. F. M. Dearborn, Metropolitan Hospital. P. L., Chinaman, aged thirty-nine years. Advanced active case of mixed type. Duration six years. Reaction: Positive.

CASE IX.—Patient of Dr. Wm. S. Gottheil, City Hospital. Chinaman, aged twenty-nine years. Moderate case of tubercular type, of four years' duration. Reaction: Weakly positive.

CASE X.—Patient of Dr. Wm. S. Gottheil, City Hospital. E. G., man, aged twenty-seven years, born in Russia. Mild case of tubercular type. Duration three and a half years. Reaction: Positive.

CASE XI.—Patient of Dr. L. Oulman, German Hospital. L. T., woman, aged twenty-four years, born in Russia. Case of mixed type of moderate severity. Duration, nine years. Reaction: Strongly positive.

CASE XII.—Colored woman, aged fifty-seven years, active tubercular case. Duration of disease four years. Reaction: Positive.

CASE XIII.—White woman, aged forty-eight years. Advanced case of mixed type. Duration fourteen years. Reaction: Positive.

CASE XIV.—White woman, aged twenty-seven years. Case of mixed type. Duration, seven years. Patient improving. Reaction: Weakly positive.

CASE XV.—White woman, aged fifty years. Mixed type of the disease in an advanced stage. Reaction: Positive.

CASE XVI.—White woman, aged forty years. Advanced and active case of mixed type. Reaction: Positive.

CASE XVII.—Colored woman, aged fifty years. Advanced case of tubercular type. Duration of disease, three years. Reaction: Positive.

CASE XVIII.—White boy, aged sixteen years. Case of tubercular type. Duration, nine years. Reaction: Positive.

CASE XIX. White man, aged forty-eight years. Incipient type, in which the disease is active. Duration, five years. Reaction: Strongly positive.

CASE XX.—White man, aged forty-five years. Advanced case of mixed type. Duration, seventeen years. Reaction: Positive.

CASE XXI.—Colored man, aged forty-eight years. Advanced case of mixed type, in which process is stationary. Duration, four years. Reaction: Positive.

CASE XXII.—Colored man, aged thirty-seven years. Active case of tubercular type. Duration, five years. Reaction: Weakly positive.

CASE XXIII.—Colored man, aged fifty years. Advanced case of mixed type. Disease active. Duration, five years. Reaction: Strongly positive.

CASE XXIV.—White boy, aged eighteen years. Terminal case of tubercular type. With active lesions. Duration, twelve years. Reaction: Positive.

CASE XXV.—White boy, aged nineteen years. Advanced case of mixed type. Duration, five years. Reaction: Positive.

CASE XXVI.—White boy, aged sixteen years. Advanced case of mixed type. Duration, four years. Reaction: Positive.

CASE XXVII.—White boy, aged twenty years. Incipient case of mixed type, relapsing after apparent cure. Duration, nine years. Reaction: Strongly positive.

CASE XXVIII.—Colored man, aged forty-two years. Terminal stage of mixed type. Duration, three years. Reaction: Positive.

CASE XXIX.—White woman, aged thirty-five years. Advanced active case of mixed type. Duration, fourteen years. Reaction: Positive.

CASE XXX.—White woman, aged fifty-seven years. Advanced case of mixed type, tubercles having disappeared. Duration, twenty years. Reaction: Positive.

CASE XXXI.—White man, aged forty years. Terminal stage of mixed type. Duration, eight years. Reaction: Positive.

CASES OF TUBERCULAR AND MIXED TYPE WITH NEGATIVE REACTION. CASE XXXII.—Patient of Dr. Wm. S. Gottheil, City Hospital. H. S., man, aged thirty-three years, born in the United States. Case of mixed type of moderate severity. Duration, ten years. Reaction: Negative.

CASE XXXIII.—Patient of Dr. F. M. Dearborn, Metropolitan Hospital. J. M., man, aged fifty years, born in Russian Poland. Case of mixed type. Very few lesions at present, though formerly well marked. Duration of disease not known. Has been in leper ward for the past six years. Reaction: Negative.

CASE XXXIV.—White man, aged twenty-eight years. Mixed type. Patient improving. Duration of disease, eighteen years. Reaction: Negative.

CASE XXXV.—White man, aged twenty-one years. Incipient case of mixed type, which is improving. Duration, six years. Reaction: Negative.

CASE XXXVI.—White man; aged twenty-four years. Advanced case of mixed type. Disease active. Duration, eighteen years. Reaction: Negative.

CASE XXXVII.—Colored man, aged twenty-six years. Terminal case of mixed type. Duration, probably five years. Reaction Negative.

CASE XXXVIII.—White woman, aged forty-three years. Case of mixed type, improving, tubercles having disappeared. Duration, twenty years. Reaction: Negative.

CASES OF MACULO-ANESTHETIC TYPE WITH POSITIVE REACTION. CASE XXXIX.—Patient of Dr. G. H. Fox, New York Skin and Cancer Hospital. T. D., girl, born in Key West, Florida. Maculo-anesthetic case of one year's duration. Reaction: Positive.

CASE XL.—Colored woman, aged sixty-four years. Incipient anesthetic case. Duration three years. Reaction: Strongly positive.

CASE XLI.—Colored woman, aged fifty-nine years. Muculo-anesthetic case, improving. Duration, two years. Reaction: Positive.

CASES OF MACULO-ANESTHETIC TYPE WITH NEGATIVE REACTION. CASE XLII.—Patient of Dr. J. McF. Winfield, Kings County Hospital. J. D., West Indian negro, aged twenty-nine years. Maculo-anesthetic type. Duration, about twenty-three years. Reaction: Negative.

CASE XLIII.—White girl, aged seventeen years. Incipient case of maculo-anesthetic type. Duration, fourteen years. Reaction: Negative.

CASE XLIV.—White woman, aged about sixty years. Anesthetic type in advanced stage. Duration of the disease, unknown. Reaction: Negative.

CASE XLV.—White woman about fifty years of age. Advanced case of anesthetic type. Duration of the disease, unknown. Reaction: Negative.

CASE XLVI.—White woman, aged about fifty years. Incipient maculo-anesthetic case. Duration unknown. Reaction: Negative.

CASE XLVII.—White woman, aged eighty-seven years. Incipient case of maculo-anesthetic type. Duration, five years. Reaction: Negative.

CASE XLVIII.—Colored woman, aged fifty-three years. Advanced anesthetic case. Duration, twenty-seven years. Disease checked. Reaction: Negative.

CASE XLIX.—Colored woman, aged about sixty years. Advanced anesthetic case, the disease being stationary. Duration, fifteen years. Reaction: Negative.

CASE L.—White woman, aged thirty-four years. Maculo-anesthetic case. Former tubercles have disappeared. Duration, eight years. Reaction: Negative.

CASE LI.—White boy, aged nineteen years. Advanced case of anesthetic type. Duration, nine years. Reaction: Negative.

CASE LII.—White man, aged forty years. Maculo-anesthetic type, improving. Duration, fourteen years. Reaction: Negative.

CASE LIII.—White girl, aged twelve years. Incipient case of maculo-anesthetic type. Duration, four years. Reaction: Negative.

CASE LIV.—Colored boy, aged nine years. Incipient case of maculo-anesthetic type. Duration, four years. Reaction: Negative.

CASE LV.—White man, aged forty-three years. Advanced case of anesthetic type. Duration, thirty years. Disease arrested. Reaction: Negative.

CASE LVI.—White man, aged fifty-four years. Incipient case of anesthetic type. Duration ten years. Reaction: Negative.

CASE LVII.—White man, aged fifty-eight years. Terminal case of anesthetic type. Duration, thirty years. Reaction: Negative.

CASE LVIII.—White man, aged fifty-six years. Terminal stage of anesthetic type. Duration, thirty years. Reaction: Negative.

CASE LIX.—Chinaman, aged seventy-five years. Anesthetic case of thirteen years' duration. Reaction: Negative.

CASE LX.—White man, aged forty-six years. Advanced anesthetic case. Patient claims to have been discharged cured from a Norwegian hospital twenty years ago. Duration, twenty-five years. Reaction: Negative.

CONCLUSIONS. 1. A positive Wassermann reaction is frequently obtained in cases of leprosy giving no history or symptoms whatever of syphilis.

2. The reaction is at times very strong, inhibition of hemolysis being complete.

3. The reaction occurs chiefly in the tubercular and mixed forms of the disease, especially in advanced and active cases.

4. In the cases of the maculo-anesthetic and purely trophic type the reaction is generally negative.

5. The value of the test is not affected in the slightest by the results found in leprosy.

In closing, I desire to express my thanks to Dr. Isadore Dyer for kindly putting at my disposal the splendid material of the Louisiana Leper Home. I also wish to thank Dr. Ralph Hopkins, the attending physician to the Leper Home for aid in obtaining case histories. For the material in New York I am indebted to the physicians whose names have been mentioned in the text.

## THE EFFECT OF TUBERCULOSIS ON INTRATHORACIC RELATIONS.<sup>1</sup>

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THE following preliminary report deals with the changes brought about in intrathoracic relations as shown by skiagrams of cases of pulmonary tuberculosis, studied clinically before and after the taking of the  $x$ -ray plates. I will confine myself simply to the more salient features of this study, which deals with the alterations in the position of aorta, heart, and diaphragm. The presence or absence, of enlarged bronchial glands, and of calcareous infiltration in the costal cartilages of the ribs is also briefly considered.

When such a study is carried out with technical precision, it would seem to leave little room for error; because with the use of the modern tubes and coils, and instantaneous exposures, the resulting skiagrams are so clear cut and definitive as to give an admirable geographical chart. I believe that such a study gives more satisfactory results in regard to the position of the organs in life than those obtained by autopsy, for in the latter there is the postmortem change, due to alteration in intrathoracic pressure or to other strictly postmortem influences; there is also the trauma of the autopsy and consequent derangement of relations, and finally there is the question of elapsed time. I feel further that purely clinical studies of this nature, when unconfirmed by röntgenology, are without much accuracy or value, except in so far as in certain instances the personal equation of the investigator has given them such.

The value of röntgenography in the study of pulmonary tuberculosis, as supplementary to physical examination, is so generally recognized as to need no exposition. I shall not discuss the use of the  $x$ -rays from the standpoint of early diagnosis, but in their relations to the later pathological changes. Röntgenology must not, of course, be considered as having solved the problems of physical diagnosis of the chest, but it helps to elucidate them and to confirm the clinical findings. It has not and never can supplant nor minimize the importance of the time-honored clinical methods, but should on the contrary serve a useful purpose in stimulating more exact methods, because the possibilities of physical diagnosis are extended from the information and suggestions gleaned from the  $x$ -rays.

The cases from which this study is made were skiagraphed by

<sup>1</sup> Read at the XVI International Medical Congress, Budapest, August, 1909.

Dr. Charles Lester Leonard, of Philadelphia, and were in some instances patients from the Pennsylvania State Dispensary, No. 21, for Tuberculosis, and in others from private practice. The majority of the cases were moderately advanced and advanced cases (Class II and III of the National Association classification), though the only selection used was in the financial ability of the patient to bear the expense of the skiagrams. The number here reported is too small (that is, 60 cases) to warrant me in drawing any very definite conclusions, but the results are at least suggestive, and the conclusions which I do present relate only to this series.

I shall not attempt at this time to discuss the data gleaned from this study, in the light of present knowledge or views, but shall content myself with merely recording the details noted, pointing out where in certain instances the conclusions drawn are at variance with the views or opinions of others.

**THE AORTA AND HEART.** It should be noted that quite frequently in advanced pulmonary tuberculosis the aorta is displaced as well as the heart and in the same direction, usually to the right. In marked displacements of the heart this is the rule (Cases II, IV, VI, XII, XIII, XXV, XXVII, XXVIII, XLVI, XLVII, LII, LIX). Rarely the aorta may be drawn out of position, while the heart is unaffected (Case XXXIII). The error is sometimes made of interpreting the physical signs of a displaced aorta, as being those of enlarged glands or of aneurysmal dilatation. With an area of dulness to the right of the sternum in the second or third interspace and much displacement of the heart, the conclusion that the aorta is displaced is warranted, in the absence of definite signs of aneurysm. Rarely an aneurysmal dilatation of the aorta may be present.

It is noteworthy that in the present series, many of which were advanced or far advanced cases, the heart in the majority of instances was not displaced. There seems no doubt about this conclusion, and I therefore feel that those who hold that displacement of the heart is a reasonably constant sign or accompaniment of pulmonary tuberculosis are in error. Turban makes the statement that "it is exceptional to find the heart in its normal position in advanced chronic tuberculosis,"<sup>2</sup> while Pottenger says that displacement of the heart is a "typical and cardinal symptom" of tuberculosis of the right apex.<sup>3</sup>

In 63.33 per cent. of the cases the heart was not displaced (that is, in 38 cases, I, III, V, VII, VIII, X, XI, XIII, XIV, XVI, XVII, XIX, XX, XXI, XXII, XXIII, XXIV, XXVI, XXVIII, XXIX, XXX, XXXII, XXXIII, XXXV, XXXVII, XL, XLI, XLIV, XLVIII, XLIX, L, LI, LIII, LIV, LV, LVI, LVII, LX).

Absence of displacement is much more common, in fact almost

<sup>2</sup> Diagnosis and Treatment of Pulmonary Tuberculosis, 1905

<sup>3</sup> Diagnosis of Tuberculosis of the Lungs, 1906.

the rule, in acute infiltrations and consolidations before fibrosis and contraction have taken place. In many instances even when the lesions were widespread and often destructive, the heart was not displaced. (Cases I, III, VIII, XI, XIII, XIV, XVI, XVII, XX, XXII, XXIII, XXIV, XXXII, XXXIII, XXXV, XLVIII, XLIX, L, LI, LVII). In Case XIII, with cavitation at the right apex and infiltration of the entire upper lobe, the heart was not displaced, due to pericardial adhesions over apex which could be plainly seen. In Case XXIII, with large cavities in both apices and much fibrosis, the heart was not displaced, possibly on account



FIG. 1.—Case XXIV. Left-sided localized pneumothorax without displacement of the heart. The case belongs to Class III of the National Association classification.

of the symmetrical character of the lesions, or possibly from adhesions. In Case XXIV (Fig. 1), with left-sided localized pneumothorax, the heart was not displaced. In Case XXXIII, with a large cavity on the right and complete consolidation of the right upper lobe, and moderate infiltration on the left, the heart was not displaced. In the following far-advanced cases with cavity the heart was not displaced: Cases XI, XIII, XIV, XXIII, XXIV, XXXIII, XLVIII, XLIX, L.

The heart was displaced in 36.66 per cent. of this series, in 15 cases to the right (Cases II, IV, XII, XV, XXV, XXVII, XXXVI,

XXXVIII, XLIII, XLV, XLVI, XLVII, LII, LVIII, LIX); in 3 cases to the left (Cases VI, IX, XXXI); and in 4 cases in the anteroposterior position (Cases XVIII, XXXIV, XXXIX, XLII), to be described later. I cannot, therefore, agree with the statement of Lawrason Brown<sup>4</sup> that "marked displacement of the heart occurs much more frequently to the left than the right."

On the contrary, when the pulmonary lesions are of fairly symmetrical character on both sides, the heart is more commonly displaced to the right than to the left (Cases II, XXV, XXXVI, LII, LVIII,



FIG. 2.—The heart in the anteroposterior position. Destructive lesions at both apices. The case belongs to Class III of the National Association classification.

LIX.) In these cases there is usually evidence to show that the primary and older lesion is on the right. When the lesion is more extensive on the left the heart is not so regularly displaced nor to the same extent, as in corresponding right-sided lesions (Cases I, III, XIV). In Case XIV, with cavity in the left apex and consolidation of the lung below, and moderate infiltration of the right apex, the heart was not displaced. Rarely the fibrosis of the lungs and pleuræ may be so great or of sufficient density to obliterate the boundaries of the heart (Case IX).

<sup>4</sup> AMER. JOUR. MED. SCI., 1908.



In 4 cases the heart occupied, what for want of a better term, I have called the anteroposterior position (Cases XVIII, XXXIV, XXXIX, XLII). In this position (Figs. 2 and 3) the heart assumes a long narrow appearance, as if it were turned upon its vertical axis. It should be noted that in all these cases, there were far advanced destructive lesions on both sides, and it might appear that the combined effect of the traction exerted under these conditions, had resulted in drawing the heart upward and inward, thus causing the apex to swing around. In long narrow chests the heart assumes a more

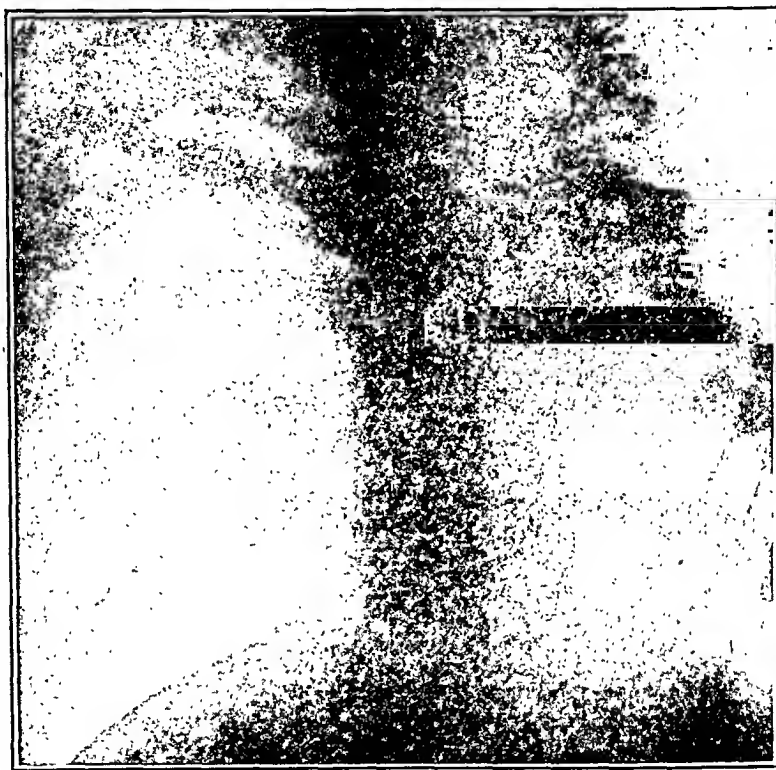


FIG. 3.—The heart in the anteroposterior position. Destructive lesions at both apices. The case belongs to Class III of the National Association classification.

oblique position. The angle formed with the liver on the right is less acute and the left boundary is appreciably more vertical. The heart also assumes an appreciably more oblique position during deep inspiration.

In many cases the skiagrams show an interesting feature which is not demonstrable clinically, namely, that during systole of the heart there is an area between the lower boundary of the heart and the diaphragm of about the extent of one centimeter, which distinctly transmits the  $x$ -rays. The limits or extent of the cardiac excursion may also be seen in many cases. In four cases, distinct

pericardial adhesions could be seen (Cases VII, XI, XIII, XVIII). The heart appeared normal in size both in the x-ray plates and to physical examination in all the cases with four exceptions (Cases XIX, XXIII, LVI, LIV). In three of these the enlargement was practically confined to the right side, and the lungs were markedly emphysematous. In Case XIX there was a general hypertrophy. There was no evidence of an organic valvular lesion in the series, though in some cases soft systolic murmurs were audible in the mitral and pulmonary areas.

**THE DIAPHRAGM.** The skiagrams were taken under full inspiration. In 29 cases (48.33 per cent.) the diaphragm was unaffected by the pulmonary lesion (Cases I, III, V, VII, X, XI, XIII, XVII, XIX, XX, XXI, XXIV, XXVI, XXVIII, XXIX, XXX, XXXII, XXXV, XL, XLI, XLIV, XLVIII, LI, LIV, LV, LVI, LVII, LX); the diaphragm was affected in this series in 51.66 per cent. of the cases. In 13 cases it was elevated on the right side (Cases II, VIII, XII, XV, XVI, XXII, XXV, XXXVIII, XLIII, XLV, XLIX, L, LVIII); in 5 cases on the left (Cases VI, XIV, XXVII, XXXI, LIII); in 7 cases it was elevated on both sides (Cases XVIII, XXIII, XXXIII, XXXIV, XXXVI, XXXIX, XLII); and in 6 cases it was not visible or determinable on account of the density of the adjacent involvement of the lungs and pleura (Cases IV, IX, XLVI, XLVII, LII, LIX).

In every case in which the heart was displaced the diaphragm was elevated on the side toward the displacement, and in the cases in which the heart assumed the anteroposterior position the diaphragm was elevated on both sides. There was one exception to this rule which does not properly apply as such, but in Case XXVII, which had been operated on for left-sided empyema some years previously, there was collapse of the chest wall, with consequent dragging upward of the diaphragm on that side, while the heart was displaced to the right.

The diaphragm was affected in 9 cases in which the position of the heart was normal (Cases VIII, XIV, XVI, XXII, XXIII, XXXIII, XLIX, L, LIII) (Fig. 4). In other words, the diaphragm was more sensitive to, or affected by, the presence of a pulmonary lesion than the heart in 15 per cent. of the cases. This was true in 5 advanced cases (Cases VIII, XIV, XXXIII, XLIX, L), as well as in 4 of the earlier cases (XVI, XXII, XXIII, LIII); and yet in 10 advanced cases in which one would have expected to find the diaphragm affected, it was not apparent (except in limitation of pulmonary excursion), either to physical examination or in the plates (Cases I, III, XI, XIII, XVII, XXIV, XXXV, XLVIII, LI, LVII). Thus in cases of relatively slight involvement the diaphragm may be elevated on the affected side (Case XXII, as type); while in cases with marked involvement and even cavitation the diaphragm may not be elevated (Case XIII as a type).

Thus the diaphragm had responded, in change of position, to the pulmonary lesion in only half the cases.

**THE PERIBRONCHIAL LYMPH NODES.** In every case in this series the cervical glands were enlarged to palpitation. It would seem probable that the peribronchial glands would also be affected in all cases, though this could not be deduced from the skiagrams. In 51.66 per cent. of the cases enlarged glands could be seen in the plates (Cases V, VII, VIII, X, XIII, XVII, XVIII, XIX, XX, XXI, XXII, XXIII, XXVI, XXVII, XXVIII, XXIX, XXX,



FIG. 4.—Showing the heart in the normal position, with the diaphragm elevated on the right. The enlarged peribronchial glands show well. The case belongs to Class I of the National Association classification.

XXXIV, XXXVII, XL, XLI, XLIII, XLIV, L, LI, LIII, LIV, LVI, LVII, LVIII, LX; 31 cases). With the exception of about 6 cases (Cases XIII, XVIII, XXIII, XXXIV, XLIII, L) all the cases in which enlarged glands were visible were either early or moderately advanced, without the breaking down of tissue; while in the large majority of the advanced cases the glands did not show. It would then appear as if there were two explanations for the absence of glands in the majority of plates in which they were not visible, namely, that their presence was concealed by the area of involvement, or what appears more likely, that with the advance

of the disease the glands had softened or broken down and so failed to give rise to a shadow. There were usually only three or four glands noted in any one plate, and in a number of instances they appeared to be calcified.

**CALCIFICATION OF COSTAL CARTILAGES.** The presence of calcareous infiltration in the costal cartilages was noted in only 8 cases (Cases I, VIII, XIII, XXVI, XLIV, LII, LVI, LVIII). It would appear to be grossly absent in many cases in which its presence might be expected and in which it could no doubt, be demonstrated microscopically; it was generally noted in the advanced chronic type of the disease, though there were exceptions to this. It was usually confined to the costal cartilage of the first rib, though in one instance it involved them all (Case VIII). In the majority of the advanced cases the involvement was of sufficient density and extent to have concealed the presence of calcification in the cartilages of the first rib, but there was no evidence of calcification in the costal cartilages which could be properly studied.

**SUMMARY OF CASES.** CASE I.—F., adult female. Infiltration of upper right lobe. Consolidation of left upper lobe. Lesion more extensive and active on left. Heart normal in position and size. No glands visible. Diaphragm not elevated. Calcareous infiltration costal cartilage first rib. (Class III, N. A.<sup>5</sup>)

CASE II.—A., adult male. Marked consolidation and fibrosis of upper half right lung, with large cavity in upper lobe. Infiltration of left upper lobe, cavity, with pneumonic consolidation left lower lobe. Heart completely displaced to right. Aorta markedly pulled over. Heart normal in size. No glands visible. Diaphragm elevated on right. Costal cartilages concealed by lesion. (Class III.)

CASE III.—H., adult male. Infiltration of right apex and left upper lobe. Heart normal in size and position. No glands visible. Diaphragm normal. No calcification of costal cartilages. (Class II.)

CASE IV.—N., adult male. Left-sided hydropneumothorax. Left lung completely collapsed. Disseminated lesions throughout right lung. Complete displacement of heart and aorta to right. Heart normal in size. No glands visible. Diaphragm not visible on left. No calcification. (Class III.)

CASE V.—O'C., boy, aged twelve years. Peribronchial infiltration on both sides radiating into apices. Peribronchial glands enlarged. Heart normal in size and position. Diaphragm normal. No calcification. (Class I.)

CASE VI.—J., adult female. Small cavity left apex with consolidation (fibroid) of left upper lobe. Slight infiltration right

<sup>5</sup> N. A.—National Association for the Study and Prevention of Tuberculosis.

apex. Heart displaced moderately to left. Aorta also displaced. Heart normal in size. No glands visible. Diaphragm slightly raised on left. No calcification. (Class II.)

CASE VII.—J., adult male. Slight infiltration on right. Early case. Heart normal in size and position. Pericardial adhesion at apex. Peribronchial glands enlarged. Diaphragm normal. No calcification. (Class I.)

CASE VIII.—J., adult female. Fibroid consolidation both upper lobes, more marked on right. Heart normal size and position. Peribronchial glands enlarged, diaphragm elevated on right. Marked calcification of all costal cartilages. (Class II.)

CASE IX.—M., adult male. Large cavity at left apex, with complete fibroid consolidation of rest of lung. Left pleura greatly thickened. Consolidation of right upper lobe. Heart not distinguishable in skiagram, clinically displaced to left. Diaphragm not visible on left. No glands visible. No calcification. (Class III.)

CASE X.—M., adult, male. Infiltration of both apices. Heart normal size and position. Peribronchial glands enlarged. Diaphragm normal. No calcification. (Class II.)

CASE XI.—S., adult, male. Small cavitation right apex, with consolidation right upper lobe. Consolidation left upper lobe. Heart normal in size and position. Pericardial adhesion. No glands visible. Diaphragm normal. No calcification. (Class III.)

CASE XII.—A., adult male. Infiltration right apex with marked fibrosis of right lower lobe. Left lung clear. Heart and aorta much displaced to right. Diaphragm much elevated on right. No glands visible. No calcification. (Class II.)

CASE XIII.—D., adult, male. Small cavity right apex, with infiltration of right upper lobe. Slight infiltration left apex. Heart normal size and position. Pericardial adhesions at apex. Glands enlarged. Diaphragm normal. Calcification first left costal cartilage. (Class II.)

CASE XIV.—R., adult, female. Cavity left apex with consolidation both left lobes. Infiltration right apex. Heart normal size and position. Diaphragm elevated on left. No glands. No calcification. (Class III.)

CASE XV.—D., adult, male. Large cavity right upper lobe, consolidation right upper lobe. Small cavity left upper lobe, with infiltration of left upper lobe. Heart displaced to right, normal in size. Diaphragm elevated on right. No glands. No calcification. (Class III.)

CASE XVI.—E., adult, male. Infiltration of both apices, more marked on right. Heart normal in size and position. No glands. Diaphragm elevated on right. No calcification. (Class II.)

CASE XVII.—V., adult, male. Infiltration both apices, more marked on right. Heart normal, size and position. Glands

enlarged. Heart normal, size and position. Diaphragm normal. No calcification. (Class II.)

CASE XVIII.—R., adult, male. Large cavity right apex, another in upper lobe, with marked consolidation of middle lobe. Small cavity left apex with consolidation of left upper lobe. Antero-posterior position of heart. Aorta displaced to right. Pericardial adhesion right side. Glands enlarged. Diaphragm elevated equally both sides. No calcification. (Class III.)

CASE XIX.—S., girl, aged seventeen years. Infiltration of right apex, marked emphysema. Heart normal position. Glands enlarged. Diaphragm normal. No calcification. General hypertrophy of heart. (Class I.)

CASE XX.—S., adult, female. Infiltration left upper lobe. Heart normal, size and position. Diaphragm normal. Glands enlarged. No calcification. (Class II.)

CASE XXI.—V., adult, male. Infiltration roots of both lungs, radiating into apices. Heart normal size and position. Diaphragm normal. Glands enlarged. No calcification. (Class I.)

CASE XXII.—D., adult, female. Infiltration right upper lobe. Heart normal size and position. Glands enlarged. Diaphragm elevated on right. No calcification. (Class II.)

CASE XXIII.—C., adult, male. Cavities both apices, with consolidation both upper lobes. Marked emphysema. Heart normal in position, enlarged to right. Diaphragm elevated both sides. Glands enlarged. No calcification. (Class III.)

CASE XXIV.—Z., adult, male. Cavity left upper lobe. Left-sided localized pneumothorax over partially collapsed lung. Heart normal in size and position. Diaphragm depressed on left. No glands visible. No calcification. (Class III.)

CASE XXV.—D., adult, male. Cavity right apex, consolidation right upper lobe. Cavity left apex. Consolidation left upper lobe. Heart and aorta much displaced to right. Heart normal in size. Diaphragm elevated on right. No glands. No calcification. (Class III.)

CASE XXVI.—J., adult, female. Infiltration both apices. Tuberculous glands of neck (operative). Heart normal in size and position. Glands enlarged. Diaphragm normal. Calcification of costal cartilage (left). (Class II.)

CASE XXVII.—S., adult, female. Left-sided emphysema (operative) complete collapse of left lung. Heart almost completely displaced to right. Aorta displaced to right. Diaphragm much elevated on left. Glands enlarged. No calcification. (Class III.)

CASE XXVIII.—P., boy. Infiltration right apex. Localized empyema on right. Fibrosis right lower lobe and pleura. Heart and aorta not displaced. Diaphragm normal. No calcification. Glands enlarged. (Class III.)

CASE XXIX.—P., adult, female. Consolidation left apex. Heart normal size and position. Glands enlarged. Diaphragm normal. No calcification. (Class I.)

CASE XXX.—U., adult, female. Infiltration right apex. Heart normal size and position. Glands enlarged. Diaphragm normal. No calcification. (Class I.)

CASE XXXI.—H., adult, female. Cavity left apex. Consolidation left upper lobe, disseminated lesions below. Infiltration right apex. Heart slightly displaced to left. Diaphragm elevated on left. No glands. No calcification. (Class III.)

CASE XXXII.—B., adult, male. Infiltration both apices. Heart normal size and position. Glands enlarged. Diaphragm normal. No glands. No calcification. (Class II.)

CASE XXXIII.—A., adult, female. Large cavity right apex, with consolidation right upper lobe. Infiltration left upper lobe. Heart normal size and position. Aorta much displaced to right. Diaphragm elevated both sides. No glands. No calcification. (Class III.)

CASE XXXIV.—C., adult, male. Cavities upper right lobe, with consolidation and marked calcification on right. Cavity left apex with marked consolidation and fibrosis. Heart in anteroposterior position. Diaphragm elevated on both sides. No calcification of costal cartilage. Calcified glands. (Class III.)

CASE XXXV.—O., adult, male. Consolidation right upper and middle lobes. Infiltration of left upper lobe. Heart normal size and position. Diaphragm normal. No glands. No calcification. (Class III.)

CASE XXXVI.—C., adult, male. Cavity at both apices, with consolidation and fibrosis of both upper lobes. Heart displaced to right. Diaphragm elevated on both sides. No glands. No calcification. (Class III.)

CASE XXXVII.—S., adult, male. Infiltration both apices. Heart normal size and position. Glands enlarged. Diaphragm normal. No calcification. (Class II.)

CASE XXXVIII.—O., adult, female. Large cavity right apex, consolidation of right upper lobe. Infiltration left upper lobe. Heart displaced to right. Diaphragm elevated on right. No glands. No calcification. (Class III.)

CASE XXXIX.—D., adult, male. Large cavity left apex, consolidation left upper lobe. Infiltration right apex. Heart in anteroposterior position. Diaphragm elevated both sides. No glands. No calcification. (Class III.)

CASE XL.—McV., adult, male. Infiltration right apex. Heart normal size and position. Glands enlarged. Diaphragm normal. No calcification. (Class I.)

CASE XLI.—R., adult, female. Slight infiltration right apex. Heart normal size and position. Glands enlarged. Diaphragm normal. No calcification. (Class I.)

CASE XLII.—T., adult, male. Large cavity right apex. Consolidation and fibrosis right upper and middle lobes. Cavity left apex consolidation, left upper lobe. Heart in anteroposterior position. Diaphragm elevated on both sides. No glands visible. No calcification. (Class III.)

CASE XLIII.—M., adult, female. Cavities in right upper lobe, with consolidation and fibrosis. Consolidation left upper lobe. Heart displaced to right. Diaphragm elevated on right. Glands enlarged. No calcification visible. (Class III.)

CASE XLIV.—McG., adult, male. Infiltration of right apex. Heart normal size and position. Diaphragm normal. Calcification of costal cartilage. Glands enlarged. (Class I.)

CASE XLV.—G., adult, male. Large cavity right upper lobe. Consolidation and fibrosis upper and middle lobes. Infiltration left upper lobe. Heart displaced to right. Diaphragm elevated on right. No glands visible. No calcification. (Class III.)

CASE XLVI.—L., adult, male. Large cavity in right upper lobe, another in middle lobe. Consolidation of lower lobe, marked fibrosis of right pleura. Consolidation left upper lobe. Heart and aorta much displaced to right. Diaphragm not visible on right. No glands visible. No calcification visible. (Class III.)

CASE XLVII.—H., adult, male. Infiltration right apex. Large pleural effusion on left. Heart and aorta much displaced to right. No glands. No calcification. Diaphragm not visible on left. (Class II.)

CASE XLVIII.—C., adult, male. Infiltration right apex. Infiltration, with cavity, left upper lobe. Heart normal size and position. Diaphragm normal. No glands. No calcification. (Class III.)

CASE XLIX.—P., adult, female. Consolidation upper right lobe with softening. Infiltration left apex. Heart normal size and position. Diaphragm up on right. No glands. No calcification. (Class III.)

CASE L.—M., adult, female. Cavity right apex, consolidation right upper lobe with softening. Infiltration left upper lobe. Heart normal size and position. Glands enlarged. Diaphragm elevated on right. No calcification. (Class III.)

CASE LI.—M., adult, male. Infiltration right apex. Consolidation left upper lobe. Heart normal size and position. Glands enlarged. Diaphragm normal. No calcification. (Class II.)

CASE LII.—A., adult, male. Large cavity right upper lobe, consolidation and marked fibrosis below. Large cavity left apex, consolidation of left upper lobe. Heart completely displaced to right. Aorta markedly displaced. Diaphragm not visible on



right. No glands visible. Calcification of costal cartilages marked. (Class III.)

CASE LIII.—G., adult, male. Infiltration both apices. Heart normal size and position. Glands enlarged. Diaphragm elevated on left. No calcification. (Class II.)

CASE LIV.—Y., adult, male. Infiltration right apex. Heart normal size and position. Glands enlarged. Diaphragm normal. No calcification. (Class I.)

CASE LV.—M., adult, male. Infiltration both apices. Heart normal size and position. Diaphragm normal. No glands. No calcification. (Class II.)

CASE LVI.—E., adult, male. Disseminated lesions in both upper lobes, marked emphysema. Heart normal in position, enlarged to right. Glands enlarged. Diaphragm normal. Calcification of costal cartilage. (Class II.)

CASE LVII.—C., adult, male. Infiltration of both upper lobes. Heart normal in size and position. Glands enlarged. Diaphragm normal. Slight calcification. (Class II.)

CASE LVIII.—M., adult, male. Consolidation right upper lobe. Infiltration left upper lobe. Heart displaced to right. Enlarged to right. Glands enlarged. Slight calcification. Diaphragm elevated on right. (Class II.)

CASE LIX.—L., adult, male. Large cavities right upper lobe, with consolidation. Marked fibrosis of lungs and pleura, right lower lobe. Cavity left apex, with consolidation upper lobes. Heart much displaced to right. Aorta displaced to right. Diaphragm not visible on right. No glands, no calcification visible. (Class III.)

CASE LX.—J., adult, female. Infiltration both apices. Heart normal in size and position. Glands enlarged. Diaphragm normal. No calcification. (Class II.)

## REVIEWS.

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THE PRINCIPLES OF PATHOLOGY. Vol. I. *General Pathology*. By J. GEORGE ADAMI, M.D., LL.D., F.R.S., Professor of Pathology in McGill University, Montreal. Pp. 948; 322 engravings and 16 plates. Vol. II. *Systemic Pathology*. By J. GEORGE ADAMI and ALBERT G. NICHOLLS, M.A., M.D., D.Sc., F.R.S. (Can.), Assistant Professor of Pathology and Lecturer in Clinical Medicine in McGill University, Montreal. Pp. 1082; 310 engravings and 15 plates. Philadelphia and New York: Lea & Febiger, 1909.

PROFESSOR ADAMI'S *Pathology* has from the date of its issue established a new standard for similar publications in America; and has lifted whatever opprobrium may have been fancied in the often repeated remark that there has been no American pathology (in the sense, of course, that the text-books of this hemisphere have followed more or less closely the thought, plan, and substance of European, notably German, authorities).

The first of these volumes, now in the second year after publication, has been widely studied; and expectancy has changed generally to cordial admiration for the breadth of fundamental discussion, the mode of presentation, and the clearness of expression of established knowledge, as well as for many of the personal views and applications introduced by the author. There have been numbers of excellent text-books issued from American presses which have not failed in matter of systematization of the subjects and in description of pathological processes and lesions; but in the endeavor to set cause to effect, to elucidate the rationale of events, and to explain the eternal "how and why" in the study of disease, the author's breadth of training and viewpoint, as well as his experience in long years of teaching, have combined to make the work notable.

A large part of this first volume is essentially preliminary, devoted to introductory consideration of the cell as a unit of vital organization, discussing the details of cellular structure and interrelation in complex organisms, our knowledge of the chemistry and physics of cellular activity, growth, multiplication, adaptation, and differentiation, and the data and problems of reproduction and inheritance. The essence of these chapters lies in the author's conception of the cellular protein molecules as elemental structures, biophores, the

various phenomena of energy being referred to changes in these; the familiar side-chain theory being applied in explanation of their constitution and their changes in metabolism. This same idea is followed in the presentation of his views of cellular growth and differentiation, of adaptation, variation, and evolution, as well as the phenomena of inheritance. The more recent publication of Reichert and Brown upon the hemoglobins of the animal kingdom, while not directly related, will be found to lend considerable confirmation to Adami's view, in that the essence of distinction in evolution, and probably, too, in all vital phenomena, whether normal or pathological, must be carried back to molecular constitution. Such views are rapidly permeating our newer conceptions of biology, since the development of physical chemistry; and are bound in the near future to dominate medicine, just as in the past, one after another, the cellular pathology and germ theory of disease bore in upon us. That new cells developing from the original fertilized ovum grow by side-chain accretions to their molecules; come to differ, as slight differences in pabulum in diverse locations obtain; and progressively diverge as the diverging products modify more and more the side-chain construction of appropriating molecules, until the complete cellular differentiation of the body, with the harmonious interdependence and mutual resistance of its cells, is established—this is basic. The protoplasmic molecule of one cell is in its general structure like the protoplasm of a cell of a different organ, or like a cell of the same part from a different animal; and the differentiation in the individual, or the evolutionary difference in different species, lies mainly in the side-chains, in their different qualities, valences, and affinities. The chromosomic theory of inheritance has never been entirely satisfying; but one can with Adami see under it in the possibilities of the chemical interaction of the complex biophores of the germ cells, a rational explanation for the dominance of one parental type, the chance for variations and mutations, and can see a reason for the only certain inheritance of acquired characteristics of the parents we know, that which follows those constitutional and toxic influences which may fixedly modify the molecular constitution of the germ cells, and in turn the progeny of these modified cells.

Thereafter, after discussion of antenatal acquirement, so often confused with true inheritance, the author devotes the remainder of the first part of the volume to the causes of postnatal acquirement of disease and the pathological processes which may logically be regarded as directly reactive or responsive to these—inflammation as a local reaction, infection with its general response in pyrexia and other phenomena, and the reactive immunity induced, as well as syncope, shock, and collapse as typifying failure of or negative reaction (death, however, being left to a subsequent section in the latter part of the volume). Of the chapters on pathogenic influences, including those of mechanical, physical, chemical, and parasitic

natures, the more notable are devoted to the endogenous intoxications from internal secretory faults and faults of metabolism and to the effects of overstrain in structural and physiological sense, and to cellular disuse.

The chapters on inflammation, after the author's well-known plan of considering the subject in a comparative manner in the simpler organisms leading up to vertebrates in order to fix the essential features of the adaptive reaction, might well stand as a type of the methods pursued throughout the volume. Whatever the injury (and the author takes the safe ground that it is by no means always of microbic origin), the two prominent factors in the process are the proliferation of the cells about the injured area and the attraction of the wandering cells to the area, the role of the bloodvessels being strictly secondary in that it really but facilitates the former. One could suggest that with these basic factors more stress might be laid upon the entrance of excess of the body fluid into the area with its general and special influences toward removal of the cause of the process; and, too, many may miss in this luminous discussion a definitive presentation of the resolution of inflammation, aside from the matter of repair and the fate of the leukocytes and fibrin, for there are additional problems in the absorption of exudate and liquid waste, in the resumption of vascular tone and similar features. Ehrlich's side-chain theory is basic to the disquisition upon immunity; but the author is not bound rigidly to an immediate and essential chemism between the antigen and antibodies, realizing the possibilities of physical relations entering into the problems afforded by the recognized phenomena and well brought forward in the later trend of study.

In the second part of the volume the familiar progressive and regressive pathological changes of less definite relation or of unknown relation to cause are presented, the author breaking away from the common habit of introducing here, however, the hyperemias, ischemia, hemorrhage, thrombosis, embolism, and œdema, reserving these for the second volume in connection with the circulatory system. The line of discussion includes in the first group hypertrophy, regeneration, transplantation, metaplasia and the neoplasms; in the second, the atrophies, abiotrophy, reversions, degenerations and infiltrations, necroses, and somatic death. In the descriptive part of each clearness and sufficiency, as may be expected, prevail; but, as in the first part of the volume, the notable features lie in the analysis of cause and relation and in the presentation, where this is impossible, of reasonable working theory. It is an open question as to the value of adding to existing morphological or relative classifications of the tumors; if it be granted, there are points of excellence in the author's separation of neoplasms into those of the lining (epithelioma) and those of the pulp tissues (myeloma), although it removes none of the difficulties in routine employment of Cohnheim's basic arrangement.

Whatever the cause of a tumor, Adami would hold there is assumed a peculiarity in its elements, not so much shown morphologically as in the predominance of a vegetative over the ordinary functioning character of the cell. Why such a character is assumed may be a matter of hypothesis, but there is reason to suppose that just as mutations in animals and plants are not mere chance, but determined more or less by alterations in environment, so it may be thought possible that cellular mutations of the type in question may by a variety of internal somatic conditions be determined, and there is no reason that stimuli of external origin, bacterial, chemical, or physical, may not do the same. He would look to no specific cause for tumors and seek for no parasite as definitely *neoformans*. The tumor cell itself is a modified body cell, and in its modification is the specific element (itself the antigen) and working out, the more atypical it is, its own antibodies from the somatic reaction to itself. Gaylord's work showing the development of immunizing substances in mice recovering from certain tumors, that of Jensen in inducing disappearance of tumor growth in mice by injecting into the animals the elements of a part of the tumor itself, as well as that of Coca along similar lines, and the recent announcement by Hødenpyl of a curative material for human cancer shown in the ascitic fluid of a cancerous human being, and other work of the same type, are all leading to a similar conclusion; and it is a safe prediction by the author that ultimate triumph over these growths is far from hopeless.

In the second volume, Prof. A. G. Nicholls collaborates with Adami. The association is valuable, no doubt, in a number of ways, but at the same time it leads to occasional lack of perfect harmony between the products of the two authors, the senior writer commonly presenting for each section an introductory portion dealing with the broad pathological problems in structure and physiological relation, and the junior author assuming the details of gross and minute anatomical description. Systemic pathology for its greater attractiveness should be presented in as fully applied form as possible, with frequent indication of the relation of the existing anatomical lesion with the symptoms manifested by the living subject, and with the distinct purpose of correlating with the primary lesions the secondary and complicating faults which invariably arise and, as a rule, prove in their combination the cause of death rather than the isolated primary lesion. Herein the authors are hampered by lack of space; and the fault in mind is not a qualitative but rather a quantitative one. It may be remedied in future editions by fuller discussion of the functional effects of at least the more important types of lesions, giving to classes of students a more certain habit of reasoning from a pathological basis in their clinical studies and at the same time insuring a more ready application of pathological knowledge by the practitioner. There is little reason for an

elaborate description of this second volume, which follows through the diseases of the blood, cardiovascular and hemopoietic organs, respiratory and other systems of the body in regular order, each with excellent anatomical exposition of its important lesions and with sections upon the broader pathological physiology of each, which are as valuable from the infrequency of such discussions in works on pathology as from their intrinsic excellence.

If, as Professor Adami says in his preface, the book was twelve years in its forming, it is worth all the time and the effort. It cannot, of course, remain indefinitely fresh: there is too rapid progress for such expectation. But it has been shaped along lines which are permanent or at least look far into the future; and is certain for its many excellences to be long-lived by repeated revision without actual recasting.

A. J. S.

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A TEXT BOOK OF PHYSIOLOGICAL CHEMISTRY FOR STUDENTS OF MEDICINE. By JOHN H. LONG, M.S., Sc.D. Second edition. Philadelphia: P. Blakiston's Son & Co., 1909.

THE subject matter of Dr. Long's book is divided into four sections: I. The Nutrients; II. Ferments and Digestive Processes; III. The Chemistry of the Blood, the Tissues, and Secretions of the Body, and IV. The End Products of Metabolism. In this edition a few changes have been made, notably the adoption of the protein classification recommended by American biological chemists, and a new chapter on the methods used in urine analysis.

One is rather appalled at the outset by being confronted with a sentence containing 134 words, of such involved construction and of such obscure meaning that if asked what he read, one might well reply with Hamlet, "Words, words, words!" The entire book while not guilty again of such verbosity, is nevertheless quite beyond the understanding of the medical student. Unless he is exceptionally well grounded in organic chemistry the book in many parts is incomprehensible, and the undergraduate who can read Chapters III and IV with an intelligent grasp of the subject is the fortunate possessor of unusual training and intellect. Chapter XIV, dealing with the complicated theme of special properties of blood serum, reflects great credit on the author. Dr. Long has presented this subject in a clear, concise, and easily understood manner, and the only adverse criticism that might be raised is that the author would have made his topic more clear had diagrammatic illustrations been shown. The chapter devoted to urinary examinations is hardly complete enough in detail for one to make even practical metabolic studies, and the index is very unsatisfactory. As a text-book the work is too lacking in explanation, and we fear the student will be unnecessarily confused by the at best recondite subject. As a laboratory book used in conjunction with practical demonstrations and intelligent instruction it may find a field of usefulness.

E. H. G.

CHEMICAL AND MICROSCOPICAL DIAGNOSIS. By FRANCIS CARTER WOOD, M.D., Professor of Chemical Pathology in the College of Physicians and Surgeons, Columbia University; New York. Second edition; pp. 725; 192 illustrations. New York and London: D. Appleton & Company, 1909.

THIS book, which comprises about the best of our knowledge on the subject, is a noteworthy addition to laboratory literature. It describes, for the most part, in good working detail, the examination of the blood, gastric contents, feces, parasites, oral and nasal secretions, sputum, urine, transudates and exudates, and milk. Some of the methods as given are lacking in essential points of description, and certain well-known tests have failed to find a place in the work under discussion. The author has chosen to give the reference where a new method was first published, and this would seem advisable in all laboratory manuals, since it is apparently impossible to find accurate record of technique in books of this nature. The plates and illustrations are uniformly good, and it is a rather novel experience to make new acquaintances in the pictorial line, instead of meeting, as has been the reviewer's misfortune in the past, one's old friends reproduced in book after book. Dr. Wood's second edition is to be heartily recommended; those engaged in laboratory practice will find it a most useful addition to an already long list of laboratory books.

E. H. G.

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LEHRBUCH DER KLINISCHEN DIAGNOSTIK INNERER KRANKHEITEN. Edited by PAUL KRAUSE, M.D., Professor and Director of the Medical Polyclinic in Bonn, Germany. Pp. 922; 360 illustrations. Jena: Gustav Fischer, 1909.

The *Text-book of the Clinical Diagnosis of Internal Diseases*, edited by Professor Krause is the composite work of thirteen collaborators. Professor Krause himself contributes chapters on the methods of examining patients, on x-ray examinations, and on clinical bacteriology; Professor Wandel, of Kiel, discusses the anamnesis and the general habitus of the patient, and the diagnosis of the acute infectious disease; Professor Lommel, of Jena, diseases of the upper air passages and exploratory puncture and cytology; Professor Gerhardt, of Basle, diseases of the respiratory apparatus; Professor Staehelin, of Berlin, diseases of metabolism, and in association with Professor Ortner, of Innsbruck, diseases of the circulatory apparatus; Professor Winternitz, of Halle, diseases of the urogenital tract; Professor Ziegler, of Breslau, diseases of the blood; Professor Mohr, of Halle, diseases of the digestive tract; Professor Jamin, of Erlangen, and Professor Finklenburg, of Bonn, diseases of the

nervous system; Professor Hertel, of Jena, diseases of the eye in internal diseases; and Professor Esser, of Bonn, diseases of infants. The book is well written, and sufficiently comprehensive, since although it includes about all that is necessary there is little if any mention of etiological factors and of matters of doubtful moment. It may be said to be representative of the present German school of medicine, and as such is to be highly commended. A. K.

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CATARACT EXTRACTION. By H. HERBERT, F.R.C.S., Late Lieutenant-Colonel, I.M.S., Professor of Ophthalmic Medicine and Surgery in the Grant Medical College, and in charge of the Sir Cowasjee Jehangir Ophthalmic Hospital, Bombay. Pp. 391. New York: William Wood & Co., 1908.

THIS work is equally valuable for its abundant citations from the writings of others who have treated of the same subject and for the fruitful lessons the author has drawn from his own experience, comprising as it does about 5000 extractions; and even this number he declares to be small compared with the work of other ophthalmic surgeons in India. The writer tells us that grave conjunctival disease is much more common in India than in Europe or America. This unfavorable condition has to be dealt with speedily and efficiently; abundant douching with bichloride solution, 1 to 3000, is the mainstay and has yielded the most satisfactory results—indeed, so satisfactory that evil is turned to good; the douchings being rarely necessary in the western world, they are omitted in the occasional cases where they would prevent infection. Of 1655 extractions, not a single suppuration occurred, certainly justifying the author's claim of a near approach to perfection in this respect. We confess to some surprise, however, at the statement that nasal infection through the lacrimal passages does not take place. The chapter descriptive of the operation, which takes up nearly one-half of the whole book, is very thorough even to minuteness. The combined operation is considered to be the standard. The capsule is divided vertically with the cystitome and the delivery of the lens is aided by fixation forceps, differently applied in accordance with special indications. Irrigation is employed when necessary to remove blood, etc. Chapter IV deals with "variations in procedure," the most valuable portion of which is the critical appreciation of the merits and faults of methods other than the writer's. There is necessarily considerable repetition here, but this is hardly a fault for the serious student.

In a work so meritorious as this one, for which the entire ophthalmic world will be sincerely grateful, it seems ungracious to seek



out any shortcomings. While we rise from perusal of the book instructed as from no other with which we are acquainted upon the subject of modern methods for operating upon cataract, we have a feeling that the subject is presented somewhat obscurely and that the reader fails to get as clear an idea of the whole as the excellent matter deserves. A little greater attention to method will easily overcome what is a fault of form but not of substance. T. B. S.

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A TEXT-BOOK OF DISEASES OF THE EAR. By MACLEOD YEARSLEY, F.R.C.S., Senior Surgeon to the Royal Ear Hospital, London. Pp. 452. Chicago Medical Book Co., Chicago, Ill., 1909.

THIS book is, as is stated in the preface, an expansion of a previous work of the author on *Common Diseases of the Ear*, but it is really an entirely new publication, and in its present form is justly entitled to rank as a very complete text-book of otology. In the arrangement, it follows the customary classification of the various subjects, although there are two useful chapters included on somewhat unusual lines, namely, Chapter XII, on the "The Influence of General Diseases of the Ear," and Chapter XV on "The Medico-legal and Life Assurance Aspects of Otology." The book is thoroughly up to date in its consideration of all the most recent developments in the science of otology. There is an excellent, though brief, account of the recent advances in our knowledge of the physiological and pathological conditions of the labyrinth. The various operations upon the temporal bone are well described, and the subject of the intracranial complications of aural disease is excellently considered. Like most English otologists, the author adopts Lake's classification of the results of tests for bone and air conduction by Rinne's method, using Greek letters as symbols for the test. To most American aurists, such a classification simply serves to complicate, and, as a rule, they prefer writing out the test result in full, to the use of an arbitrary symbol. The illustrations throughout the book are generally original, and of most excellent quality. It can be safely commended to the student of otology as an excellent epitome of the subject. F. R. P.

# PROGRESS OF MEDICAL SCIENCE.

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## MEDICINE.

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UNDER THE CHARGE OF

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**The Effect of Digitalis on the Ventricular Rate in Man.**—Of the cardiac irregularities produced experimentally by digitalis, the earliest to appear is usually an occasional omission of ventricular contractions, owing to the blocking of the stimulus from auricle to ventricle. A somewhat late phenomenon is the production of a complete auriculoventricular dissociation which differs from ordinary heart-block in that the ventricular rate is not slow, but approaches, and usually exceeds that of the auricles. Although a common result of digitalis poisoning in dogs, this condition has never been noted in man except in the case reported by HEWLETT and BARRINGER (*Arch. Int. Med.*, 1910, v, 93). Their patient, a man, aged twenty-seven years, with chronic myocardial insufficiency, who had taken digitalis in moderate doses over a considerable length of time, developed on the day before his death, a remarkable condition. Tracings of the venous pulse and apex showed a regularly recurring cycle of changes apparently depending on the interference of two systems of waves which were independent of each other, and not quite synchronous. Each cycle lasted about seven seconds and included fourteen ventricular contractions. The two systems of waves were evidently due to the auricular and ventricular contractions, and the rates were such that for thirteen auricular there were fourteen ventricular contractions. Hewlett and Barringer believe this to be the result of a cumulative action of the digitalis, and call attention to the fact that it may be difficult to ascertain when enough of the drug has been given, for at no time was there a slowing of the pulse. While in experimental heart-block the rate of the ventricle is increased by digitalis, there is little clinical evidence on the subject. In a case of complete heart-

block with slow pulse, however, the same writers failed to note any increase of ventricular rate after the use of moderately large doses of digitalis. It is possible that the appearance of extrasystoles and the temporary disappearance of the *a* waves from the jugular pulse (due to a toxic weakening of the auricular contractions?) may have been due to the drug.

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**Auricular Fibrillation.**—It is well known that in the latest stages of cardiovascular degeneration, especially in mitral stenosis, the pulse often becomes exceedingly irregular, and in the jugular the wave of auricular contraction disappears. This has long been regarded, particularly by Mackenzie, as depending upon the origin of the rhythm at the node of Tawara (hence the term nodal rhythm). LEWIS (*Brit. Med. Jour.*, 1909, ii) asserts that facts are at his disposal permitting the conclusion that the rhythm arising in the neighborhood of node gives rise to a different clinical picture. This conclusion is based upon the study of an instance of paroxysmal tachycardia in which auricle and ventricle contract together. Secondly, the *pulsus irregularis perpetuus* is dependent upon fibrillation of the auricle. This conclusion is based upon the fact that the rhythm is exactly similar to that which may be produced experimentally by inducing fibrillation of the auricle, and is a unique condition. Lewis points to the fact that electrocardiograms taken from patients exhibiting this irregularity, show a number of irregular waves apart from the ventricular curve, and more clearly defined in diastole. Such waves are found in no other disorder of the heart action. They disappear when irregularity vanishes, are not evident upon the cardiogram, and are identical with the curves yielded by fibrillation of the auricle. Furthermore, synchronous tracings show that the waves in the experimental cardiogram correspond to the fibrillary movements of the auricle. [In connection with this interesting communication it may be remembered that CUSHNY and EDWARDS in the *AMERICAN JOURNAL OF THE MEDICAL SCIENCES*, 1907, cxxxiii, 66, arrive at the conclusion that an instance of paroxysmal irregularity was probably due to this cause.—W. S. T.]

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**The Etiology of Beri-beri.**—The studies of FRASER and STANTON at the Institute for Medical Research, Federated Malay States (*Trans. Soc. Tropical Med. and Hygiene*, 1910, iii, 257), are based on the chemical analyses of various types of rice, and on the production of polyneuritis gallinarum, a disease analogous to beri-beri, by feeding experiments in fowls. It was first found that Siam rice, which is most often associated with epidemics of beri-beri, contains a lower percentage of fat, than either Rangoon rice or parboiled rice. Microscopic sections showed that in Siam rice the pericarp, the outer layer, containing most of the aleurone and oily material, had been removed by the process of polishing. The relation of the milling of rice to the production of the disease in fowls was then studied. Fowls fed on the original padi ale remained healthy. Of twelve fowls fed on the finished, polished rice, six developed polyneuritis. Other fowls fed on the same finished rice, plus the polishings, all remained healthy. From these experiments Fraser and Stanton concluded that the polishing of white rice removes from the seed some substance essential to the maintenance of the

normal nutrition of nerve tissues. It was further shown that staleness of rice, or the development in it of poisonous substances subsequent to its being milled are not important factors. Parboiled rice, in itself healthy, when extracted with alcohol, caused polyneuritis in fowls, but the addition of the alcoholic extract to a rice known to be injurious prevented this disease. Further chemical investigations showed that the power of a rice to produce polyneuritis gallinarum varied with its phosphorus content—the higher the phosphorus content, the less liable was it to be injurious. The highest percentage of phosphorus was found to be present in rice polishings. Moreover, the addition to an injurious rice of a quantity of polishings which contained enough phosphorus to bring the total phosphorus content up to that of parboiled rice sufficed to preserve nutritive equilibrium. The prevention of beri-beri thus depends on the substitution of ordinary white rice, by a rice in which the polishing process has been omitted, or carried out to a minimal extent, or by the addition to a white rice diet of articles rich in those substances which are not present in sufficient amount in white rice. One such article, which is cheap, and may be readily obtained, is the polishings from white rice.

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**The Physiology of the Immediate Reaction of Anaphylaxis.**—On the injection of a dose of horse serum into the vein of a previously highly sensitive guinea-pig, there occurs a chain of symptoms—chiefly of respiratory nature, which result in the death of the animal in from three to five minutes. While the general type of the reaction has been reported and confirmed by various observers, it has remained for AUER and LEWIS (*Jour. Exper. Med.*, 1910, xii, 151) to study and explain the physiological basis. While convulsive and paralytic symptoms may dominate the picture if the animal is loose, they found that if it is held in a suitable holder these are less marked and the respiratory changes come into the foreground. They thus paid especial attention to the lungs, and found, as did Gay and Southard, that at autopsy the lung in acute anaphylaxis tends to remain in an inspiratory, distended condition with open thorax, with unobstructed trachea, and large bronchi, and without obvious pulmonary oedema. This immobilization of the lungs they consider to be the most characteristic sign of immediate anaphylaxis in the guinea-pig. Experiments were performed in which the respiratory movements of the chest and the volume changes of the pleural cavity were recorded, as well as others in which the animals were allowed to breathe from a bottle, and changes during inspiration and expiration registered. As a result it was evident that some stenosis is gradually produced in the pulmonary passages so that in the final stage practically no air enters or leaves the lung in spite of violent respiratory attempts. Death is due to asphyxia. The characteristic reaction of anaphylaxis was also obtained in pithed animals, showing that its production depends on a peripheral process in the lung, and not on the central nervous system. After reviewing the possible cause of the condition, the authors conclude that it is due to a tetanic contraction of the muscles of the finer bronchioles, so that air is imprisoned in the areolar sacs. Atropine, which paralyzes the bronchial muscles, may, under certain conditions, be able to relax the anaphylactic lung so that it is again able to expand and contract. The blood pressure

in immediate anaphylaxis first shows a considerable rise, and then a gradual drop to 10 to 20 mm. Shortly after the injection of the toxic dose, a heart block, often with a 3 to 1 rhythm, develops, and is probably due to asphyxia. The cardiac vagus gradually loses its irritability after injection of the toxic dose.

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**Jaundice in Pneumonia.**—As a result of the experimental study of cholecystitis, LEMIERRE and ABRAMI have previously shown the important part played by descending, hematogeneous infections in the production of inflammation of the bile passages. They now (*La presse méd.*, 1910, No. 10, 82) report three fatal cases of pneumonia associated with jaundice in which bacteriological examination of the bile at autopsy showed pure cultures of pneumococcus. In all three instances the stools were colorless, but careful search revealed no obstruction in the bile passages. The fluid in the gall-bladder was nearly colorless, and in two of the cases failed to give a Gmelin reaction. They believe that the primary cause of the jaundice is an involvement of the liver parenchyma, and that any inflammation of the bile ducts is purely secondary. In all of the cases there were signs of alcoholic cirrhosis of the liver, and Lemierre and Abrami consider that hepatitis complicating pneumonia is rare except when the liver has been the seat of some previous pathological process.

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**On the Quantity of Glycuronic Acid in the Urine in Health and Disease.**—TOLLENS and STERN (*Hoppe-Seyler's Ztschr. f. physiol. Chemie*, 1910, lxiv, 39) have found, by means of a new quantitative method recently described by Tollens, that the excretion of glycuronic acid in the urine is far greater than has generally been supposed. Mayer and Neuberg, for example, give the daily average output as 0.004 gm. per 100 c.c., whereas the authors find 0.025 gm. per 100 c.c. or 0.3 to 0.4 gm. in the twenty-four hours' urine as the average in health. In several cases of diabetic coma, they have encountered a complete absence of glycuronates in the urine, tested with the naphthoresorcin test. Administration of sodium salicylate, which causes a marked augmentation of the glycuronates in the urine as a rule, failed to produce a positive reaction in these cases. Various drugs, especially salicylates and chloral hydrate, combine with glycuronic acid in the body; after their administration, the glycuronic acid may amount to 1.4 gm. per diem. In one case of carbolic acid poisoning (25 gm.? taken) the urine, blackish green in color and definitely levorotatory, contained 8.5 gm. of glycuronic acid on the first day. Such a urine, of course, is capable of reducing Fehling's solution.

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**The Cultivation of the Organism of Infantile Paralysis.**—It is of interest in relation to the recent publications of Flexner and Lewis on the etiological factor of anterior poliomyelitis, to receive the results reported by LEVADITI (*Presse médicale*, 1910, No. 6, 44) in a preliminary note from the Pasteur Institute. In several experiments he has inoculated bouillon to which the blood serum of monkeys and rabbits has been added, with active filtrates containing the specific organism. In one instance the medium became cloudy after being kept in the thermostat for ten days. At the end of fifteen days the culture was injected into a monkey. After

an incubation period of twenty days paralysis set in, thus demonstrating that the organism retains its virulence for at least fifteen days at 38 degrees. Microscopic examination of the cloudy medium by ordinary methods showed no micro-organisms, but after centrifuging, dissolving the clot and mordanting after fixation by alcohol or heat, he was able to find a large number of round or rather oval bodies, appearing in pairs or in masses. They are extremely small and are sometimes polymorphous. They do not stain well with aniline dyes, but after prolonged staining with dilute fuchsin assume a pale pink color, or appear as clear dots surrounded by a pinkish zone. Control experiments with culture media which had not been inoculated showed only granules of quite different size and shape.

**Rat-bite Fever.**—HORDER (*Quarterly Jour. of Med.*, 1910, iii, 121) has collected three instances of an apparently specific kind of blood-poisoning following the bite of a rat. The most prominent symptom noted was periodic fever beginning from twenty-one to twenty-eight days after the occurrence of the bite. The temperature rose to 103° to 104°, fell to normal in two to three days, and then rose again in the course of the next few days. In one case the remission continued over several months. During the febrile periods there was a well marked leukocytosis. In two instances there was a blotchy erythema, and in one of these indurated plaques and diffuse tender subcutaneous nodules were present. Blood cultures and the inoculation of blood into animals gave no results and the examination of stained specimens of blood failed to reveal any parasites. There was no enlargement of the spleen. The prolonged incubation period, the form of the fever and the absence of suppuration in the original wound make it unlikely that the cause of the disease is a pyogenic infection secondary to the bite. Horder considers that the etiological factor is probably a protozoon. [It is interesting to note that QUINCKE (*Mitt. aus. d. Grenzgebiet, d. med. u. Chir.*, 1900, v, 231) has reported eleven cases of almost exactly the same symptom-complex which occurred in Japan. He also refers to a number of articles in the Japanese literature, and states that while there is no mention of it in European literature, a characteristic remittent febrile disease following the bite of a rat after a more or less prolonged incubation period, has been recognized in Japan for many years.—W. S. T.]

**"Nail-palpation" of the Arterial Wall.**—WERTHEIM-SALOMONSON (*Deut. Arch. f. klin. Med.*, 1910, xeviii, 596) calls attention to the well-known difficulties of palpating the arterial wall (1) where the arterial wall is thin, (2) when it is densely covered with fat, and (3) when the blood pressure is high. He proposes a method, which he calls "nail-palpation" (Nagelpalpation), by means of which any arterial wall, whether it can be palpated in the usual way or not, may be felt, and its thickness fairly well judged. Instead of palpating the artery with the ball of the finger, the finger-nail is used. The nail is placed perpendicularly on the surface of the skin, so that the edge of the nail runs parallel with the long axis of the artery. By moving the finger transversely across the artery, the latter slips under the nail as if it were dissected out. The artery may be palpated in this way almost as readily in young children as in adults. With a little practice, Wertheim-

Salomonson says one quickly learns to recognize arterial thickening. The method is applicable to the palpation of any artery which rests on a firm bed, as well as to the palpation of many superficial nerves.

**A Previously Undescribed Symptom of Tetany.**—H. SCHLESINGER (*Wien. klin. Woch.*, 1910, xxiii, 315) has observed a new sign in a typical case of tetany, which he designates the "Beinphänomen." The sign is elicited in the following manner: If one seizes the leg with the knee joint extended and then flexes the thigh on the abdomen, in a short time (at the most, two minutes) an extensor cramp develops in the knee with extreme supination of the foot. The phenomenon may appear when the patient sits up in bed. If the trunk is flexed on the thighs, the spasm likewise appears. Like the Trousseau phenomenon, the new sign can be brought out in the intervals between attacks. The frequency of occurrence of the Beinphänomen in tetany cannot be foretold as yet; nor is it known that the sign is one peculiar to tetany.

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## S U R G E R Y.

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UNDER THE CHARGE OF

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**Atlo-axoid Fracture Dislocation.**—PILCHER (*Annals of Surgery*, 1910, li, 208) reports a case which has been under his care for a period of nearly ten years, and therefore represents the possibilities of ultimate repair and restoration of function which may take place in such cases. The patient, a man, aged thirty-three years, fell headlong a distance of fifteen feet, striking on his forehead. His head was notably bent over toward his left shoulder and was fixed in such great flexion that he could not open his mouth more than a half-inch. He had no symptoms other than suboccipital pain and the deformity and stiffening of the neck. During the following two months he was conscious of a growing lack of power in his lower limbs, most marked on the right side. Shortly afterward it was found that he had no power in his right arm or leg, except a little in the fingers and toes. Catheterization became necessary. Pileher saw him first about three months after the injury, and six weeks later the atlas and axis were exposed by operation. A forward dislocation of the atlas upon the axis was demonstrated, but careful attempts to reduce it were futile and the wound was closed. A slight improvement developed in the subsequent weeks. He became able to empty his bladder spontaneously and two months after the operation

began to sit up. He was still hemiplegic when he left the hospital ten weeks after the operation. A gradual return of power in the paralyzed leg manifested itself after his return home and continued until the normal condition returned. Less improvement occurred in the right upper extremity. Nine years after the accident the deformity of the head and neck and the immobility were unchanged. He is able to walk normally fairly long distances without fatigue. There is no differences in strength between the two lower limbs. The bladder function is normal and his mentality is unaffected.

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**Malignant Degeneration of Benign Diseases of the Breast.**—SPEESE (*Annals of Surgery*, 1910, li, 212) follows Warren's classification. He finds that certain tumors which present symptoms of malignancy do not show malignant histological changes, and, on the other hand, carcinoma occasionally arises in a preëxisting tumor without causing symptoms indicative of such a transformation. It is concluded that operative interference in all tumors of the fibroepithelial type, is indicated to prevent this complication. Two instances of carcinomatous changes were found in 17 cases of periductal fibroma studied pathologically. In both there were one or two symptoms which were only suggestive of cancer. Abnormal involution (chronic mastitis) occurs more frequently than any other affection of the breast with the exception of carcinoma. In 180 cases of breast disease, Speese found it in 18 per cent., and of the 35 cases studied in the laboratory, 9 instances of malignancy were encountered (26 per cent.). In 295 cases of abnormal involution reported by 9 different writers 44 were found to be carcinomatous (15 per cent.). In doubtful cases exploratory incision is indicated; a careful search throughout the entire part involved is necessary, for the malignant area is apt to be small. Malignancy being detected, a radical operation should be performed. The exploratory incision does not reduce in any way the chance of ultimate cure, whereas exploratory incision followed by the radical operation for malignancy at a later period has been invariably fatal according to Bloodgood. The bilateral character of the disease is one of the interesting features and one for which occasional double amputation has to be performed. Cystadenomas, cancer cysts and mastitis are also discussed. Areas of induration following mastitis should receive as careful attention as other forms of benign disease, early removal of which may remove its greater danger.

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**The Treatment of Cystitis, Especially, Severe Postoperative Cases.**—SCHLAFI (*Zeit. f. Gyn. u. Urol.*, 1910, ii, 4) says that in most cases he has not used irrigations but has depended chiefly upon internal therapy, with flushing and disinfection from within. For urinary antiseptics he has employed aspirin, benzosalin, novaspirin, and diplosal. Of these the most effective was aspirin. When irrigations were employed the quantity injected was never so great that it distended and irritated the bladder walls. It was given slowly and regularly and the temperature of the fluid was usually between 18° and 20° C. Only somewhat persistent acute and subacute catarrhal conditions and especially severe pus cases, make irrigation necessary. Aniodol was found to be the best antiseptic solution for the irrigation. It is a formaldehyde preparation with some sulphozyanallyl. Its bactericidal properties are greater than



that of other urinary antiseptics. According to Fouard's investigations it can be said that it gives the greatest therapeutic effect with the least danger, since it is neither caustic nor toxic like sublimate and carbolic acid. Schlafi used it in a 0.25 per cent. solution, which gave it a sufficient concentration and produced no symptoms of irritation. It has simplified the treatment of cystitis. It provides for the mechanical cleansing, and the removal of the decomposed urine and its contained pus; and it provides the best bactericidal effect without the disadvantages of other equally strong disinfectants.

**The Operative Treatment of Wounds of the Lungs.**—MÖLLER (*Archiv f. klin. Chir.*, 1909, xci, 295) says that up to a few years ago penetrating wounds of the thorax involving the lungs, were generally treated conservatively, with rest in bed, morphine, ice, and antiseptic treatment of the wound. A simple occlusive dressing, or incision and tampon of the wound in the thoracic wall or suture of the wound was employed. For some years efforts have been made to find the lung wound, through a sufficient opening in the chest wall, and to suture or tampon the wounded lung surface. Stucky reported 25 cases of wounds of the lungs treated by suture, and concluded that in every stab wound of the thorax coming into the hospital within twenty-four hours after the accident, the ribs should be resected, the lung wound exposed and sutured. This led to the collection and study of similar cases from Körte's clinic, from which it was determined that the radical operation proposed by Stucky, not only was not necessary, but was improper; and that these wounds healed with simple occlusive dressing. In some few severe cases free exposure and direct treatment of the lung were justified. The material studied consisted of 90 cases in which the pleura and perhaps the lung were wounded, 48 by gun-shot, 19 by stab or incision, and in 23 there was a subcutaneous laceration of the lung, 12 with and 11 without a fracture of the ribs or sternum. Of the 48 gun-shot cases, the symptoms occurred as follows: Hemothorax, 37 times; hemoptysis, 21 times; pneumothorax, 12 times; and connective tissue emphysema, 9 times. The treatment and course were as follows: Puncture and aspiration, 10 times; empyema, 4 times; rib resection, twice; excision of the shot, 14 times. Death resulted in 7, and the average duration of healing was five to five and one-half weeks. The following complications occurred: Wound of the pericardium in 5, of the heart in 2, of the diaphragm and abdominal organs in 2, and of the spinal canal in 1. Of the 19 stab wound cases, the prominent symptoms occurred as follows: Hemothorax in 9, hemoptysis in 3, pneumothorax in 7, and emphysema in 8. Puncture and aspiration were employed in 2, and the average time of healing was three and one-half to four weeks. Wound of the pericardium occurred in 2 cases. Of the 23 cases in which subcutaneous rupture of the lung occurred without wound of the thoracic wall, the symptoms were as follows: Hemothorax in 3, hemoptysis in 4, pneumothorax in 1, and emphysema in 8. Death occurred in 7, and the average time of healing was four weeks. The complications were: Fracture of the skull in 1, rupture of the liver in 1, and wound of the kidney and hematuria in 1. Of the 7 deaths in the 67 penetrating wounds, in only 2, or at most 3, cases, was the question of operation presented. Of Stucky's 25 stab wounds, all of which were operated on, death occurred

in 9, abscess of the lung or empyema in 12, and the average time of healing was ten weeks. In Möller's 19 stab wounds which penetrated the lung, none died, in none was there suppuration, and the average time of healing was three and one-half to four weeks. Möller gives the indications for operation as follows: Severe primary hemorrhage; continuing and repeated hemorrhage; severe pneumothorax and emphysema; and secondary pneumothorax. With the observance of these indications, the prognosis of these cases in the future should be somewhat better than they have been up to the present with conservative treatment.

**Stasis Hemorrhages Resulting from Compression of the Thorax and Abdomen.**—Koch and Ronne (*Archiv f. klin. Chir.*, 1909, xel, 371) reports a case in which a man was severely compressed in an elevator accident. Immediately after the accident his appearance was alarming. His head and neck were very cyanotic, of a dark blue, almost black, color, and he had small and large petechial hemorrhages under the skin everywhere. The head was swollen out of shape and the breathing was almost imperceptible. The skin of the neck projected over the collar of the clothing, the eyes protruded, and there were subconjunctival hemorrhages. In striking contrast to these phenomena was the slight effect on the general condition. Very often these patients are completely conscious during the whole period of the compression of the chest and abdomen. The cyanosis disappears in a few days, the small hemorrhages somewhat later, the subconjunctival hemorrhages remaining perhaps several weeks. If no complicating lesions are present, in a few days the patients probably feel sound. In 58 collected cases, in only 7 did the complications produce a fatal result. The most probable explanation of the phenomena is that with a closed glottis the blood of the lungs and heart is forced into the peripheral vessels. The cyanosis is very marked in the head and neck and very rare in the extremities, because the jugular veins have no valves. They are occasionally insufficient in the axillary, but are very resistant in the veins of the lower extremities. Disturbances of sight are common, often without demonstrable cause ophthalmoscopically. They were present in 11 (12 with the case here reported) out of the 58 cases. Occasionally there is a brief double blindness, which lasts for some minutes or a half hour. In other cases sight does not return or does so only incompletely, and after some time an atrophic discoloration of the papillæ develops showing that the nerve fibers have become degenerated.

**An Experimental and Literary Study Concerning the Manner and Pathway of Extension of Urogenital Tuberculosis.**—Sawamura (*Deut. Zeit. Chir.*, 1910, ciii, 203) in investigating the method of extension, assumes that in primary urogenital tuberculosis, the process begins in the kidney and extends through the ureter to the bladder and prostatic urethra, and through the vas deferens to the testicle. It may begin in the testicle and extend in the reverse direction, or beginning in the seminal vesicles, it may extend in both directions to the testicles and kidneys. Upon the basis of the literature it is agreed that the process often begins in the kidney and that the bladder may, in time, be infected, although a sound mucous membrane can, to a certain extent, protect the bladder. Tubercle bacilli in the bladder, usually, will not infect the kidney, if

the normal stream of urine is not obstructed, but will do so in the presence of such obstruction. When tubercle bacilli are injected into the ureter, especially, into the renal pelvis, tuberculosis of the kidney can be produced, with or without ligation of the ureter, although the latter undoubtedly favors its development. The infection must pass by the blood, lymph, or ureter. The blood path is excluded from consideration because by it is produced usually a general tuberculosis. Sawamura carried out experiments on dogs to determine the path of extension. He failed to find that the tubercle bacilli ascended from the bladder through the ureter to the kidney. By direct injection of the bacilli into the lumen of the ureter, without subsequent occlusion of the ureter, a renal tuberculosis was produced. Extending by the lymph paths to the kidney, vesical or genital tuberculosis rarely invades the kidney. It may ascend from the bladder to the kidney without obstruction of the blood stream, when from contraction of the bladder a relatively high internal pressure is produced and in any manner an antiperistaltic movement of the ureter occurs. Tuberculous involvement of the lower end of the ureter may produce the necessary obstruction, stagnation, and dilatation, to permit the tubercle bacilli to reach the kidney. That the process may ascend by the lymph paths cannot be denied, although it has never been established in men or animals with certainty. Tuberculosis of the testicle or epididymis, as a rule, extends through the vas deferens toward the urethra. More rarely it may extend by the lymph vessels. It may remain localized in the testicle and epididymis. Often the vas is involved. The lymph vessels of the testicle go chiefly to the nodes along the inferior cava, near the entrance of the spermatic vein; those from the epididymis to the nodes along the hypogastric vessels. The central (lying next the urethra) portion of the vas deferens, may become infected from tubercle bacilli in the urine. Tuberculous epididymitis can develop from tubercle bacilli in the urine by way of the vas deferens, provided the orifice of the vas or its lumen is blocked, so that with the stagnation of the secretion and exudate, the tubercle bacilli are transported to the epididymis. Extension from a tuberculous epididymis, without participation of the vas deferens, did not occur in Sawamura's experiments, although Oppenheim, and Law and Hausen considered this possible. A primary focus of tuberculosis can develop in the prostate. It may involve the seminal vesicles and it is assumed, therefore, that it may extend to the epididymis. The seminal vesicles may be involved alone. Sawamura believes that in dogs an ascending tuberculosis of the female genitals can occur.

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**The Treatment of Bone and Joint Tuberculosis by the X-rays.**—ISELIN (*Deut. Zeit. f. Chir.*, 1910, ciii, 483) had already obtained excellent results in the treatment of tuberculosis of glands and other soft tissues. Two years ago, at the request of his chief, Prof. Wilms, he undertook the same treatment of the bones and joints. In all, 41 cases were treated, including the bones and joints of the hand, foot, elbow, knee, sacro-iliac joint, and ribs. The method was as follows: In the beginning of the treatment, the bone or joint was exposed to the x-rays, three or four times at short intervals, every exposure being made from a different side and always with the fullest dose, until all parts had been exposed. The rays were passed through an aluminum plate, 1 mm.

thick. Because the effects on the skin did not show until two or three weeks, the exposures were made only every three or four weeks. More than three such exposures were unnecessary. From the beginning the joints were placed in a position favorable for cicatricial contraction, except in the case of the small joints. If the tuberculosis healed by cicatrization, after treatment was necessary to reproduce the mobility. This consisted of exposures to hot air, massage of the joints, and movements. This kind of healing was obtained in 10 cases of bone and joint tuberculosis. Almost always the progress was visible, and was obtained in many otherwise hopeless cases. The method is not suited to children, because the epiphyseal cartilage can be damaged, and in the large joints of adults, as the shoulder and hip, the x-rays could not be made to penetrate deep enough.

## THERAPEUTICS.

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**Diet in Typhoid Fever.**—COLEMAN (*Jour. Amer. Med. Assoc.*, 1909, liii, 1145) advocates a more liberal diet in the treatment of typhoid fever. He says that the average milk diet of two quarts daily supplies an insufficient number of calories to provide for the increased needs of the body. Consequently patients on a milk diet lose weight and strength and are less able to cope with the disease than patients on a more liberal diet. Coleman advises, as the minimum requirement, a diet containing the equivalent of 41 calories per kilo of body weight. Thus, a man weighing one hundred and fifty pounds will receive during the twenty-four hours a diet equivalent to 3000 calories. Coleman and Shaffer found that the best results were obtained when the diets furnished 60 to 80 calories per kilo. In all instances, the patients on a liberal diet were brighter and stronger and better able to fight the disease. The principal constituents of Coleman's diet are milk, cream, milk sugar, and eggs. In addition, small slices of stale bread or toast, with as much butter as the patient wished, were allowed. He gave to his cases one and one-half quarts of milk, from one to two pints of cream, from one-half to one and two-thirds pounds of milk sugar, and from three to six eggs. Coleman says that he has seen no bad effects from the use of milk in moderate amounts, and he does not believe that it increases the tendency to tympanites. A quart of good milk is equivalent to about 740 calories. Coleman furnishes the bulk of the fat in his diet by means of cream. It is not advisable to give more than one-third of the total calories in the form of fat. A pint of cream contains about 1300 calories. Some of the patients were able to take as much as two pints of cream, but when the larger quantities cause diarrhoea the amount of cream in the diet must be diminished. Carbohydrates protect body

protein better than any other foodstuff. For this reason Coleman supplies a large quantity of the energy of his diet in that form. Starches cannot be used in quantity because of their bulk and the consequent tax on the digestive organs. He prefers milk sugar because it is not very sweet and not so likely to disgust the taste as other sugars, and because it does not so readily produce digestive disturbances. The objections to its use are that in some patients it produces nausea and vomiting, but more often vomiting without nausea. When vomiting occurs, the milk sugar should be stopped. In a few cases milk sugar caused tympanites, but usually the patients could be gradually taught to take and assimilate large amounts. An ounce of milk sugar is equivalent to 120 calories. Milk sugar may be given in the milk; in coffee, tea, or coca, in lemonade, or in custard made with milk and egg. Coleman and Shaffer found that in order to maintain nitrogen equilibrium from 12 to 16 gm. of nitrogen are required in the diet. Approximately 11 gm. are contained in one and one-half quarts of milk and one pint of cream. Coleman supplies the deficiency in nitrogen with eggs. A two-ounce egg will supply 1+gm. nitrogen. The details of administering the diet may be modified to suit the individual case. Coleman gives as a working basis six ounces of milk with two ounces of cream every two hours. From one to four tablespoonfuls of milk sugar are added to the milk and cream mixture. The eggs may be given soft-boiled, poached, or raw in milk with or without whiskey.

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**Antidiphtheritic Serum and Antidiphtheritic Globulin Solutions.**—PARK (*Jour. Amer. Med. Assoc.*, 1910, liv, 251) says that until recently the only means of giving diphtheria antitoxin was in the whole serum of the horse in which it had originated. Lately a practical method has been developed to eliminate a portion of the non-antitoxic serum substances while retaining the antitoxin. Park gives a brief description of two globulin preparations containing diphtheria antitoxin. He also points out the fact that the blood serum from different horses varies not only in antitoxic potency, but also in its liability to produce disagreeable after-effects. Thus, different lots of serum of the same manufacturer will vary in liability to produce rashes, and this, together with the idiosyncrasy of the patient, causes some physicians to approve and others to condemn the preparations of the same manufacturers. Park compares the effects of antidiphtheritic serum with those obtained by the globulin preparations. He believes that the globulin preparations contain all the important substances of the whole antidiphtheritic serum. He also states that the rashes and after-effects, in cases observed by him, were undoubtedly much less after the Gibson injections than after the whole serum, and somewhat less after the injections of the Banzhaf modification than after that of Gibson. Curiously enough, only certain types of rashes are eliminated. The urticarial reactions still frequently follow.

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**Tuberculin Treatment of Tuberculosis.**—LÖWENSTEIN (*Therap. Monats.*, 1909, xi, 593) used Koch's "old" tuberculin in the treatment of 300 cases of open pulmonary tuberculosis at the Beelitz sanatorium. He commences with a dose of 0.0002 gm., being convinced that smaller doses are liable to induce anaphylaxis. In case of a strong general reaction

with focal phenomena, he waits fourteen or eighteen days before resuming the treatment. After a milder reaction he waits seven to ten days. When the doses of tuberculin have reached 0.1 gm., the intervals between injections should be at least ten days. He does not reduce the dose after a reaction, but increases it more or less according to the intensity of the reaction. Löwenstein terminates the treatment when the patients can stand 0.5 gm. without reaction. In order to avoid a considerable general or local reaction, Koch's "bacillen emulsion" is given instead of the "old" tuberculin. Löwenstein advocates the use of tuberculin in every case in which the physician thinks improvement is possible. He says he has used tuberculin in 1000 cases, and has never observed a dangerous hemorrhage that could be ascribed to the influence of the tuberculin injections. He gives as contra-indications to the use of tuberculin, persistent headache, pointing to the localization of the infection in the central nervous system, nephritis, unless of tuberculous origin, diabetes, epilepsy, and pregnancy.

**The Treatment of Gastropnoia.**—VON NOORDEN (*Therapie d. Gegenwart*, 1910, i, 1) believes that the chief indication in the treatment of gastropnoia is to improve the nutrition of the patient. The falling of the stomach is not only a result of stomach atony, but is also due to the lack of support from thin and relaxed abdominal walls. The stomach must never be overloaded, and he advises small and frequent meals of high nutritive value. Solid and fluid food should not be taken at the same time. He advises as an important part of the treatment that the patient should lie down after the principal meals, with the body turned slightly toward the right side. Von Noorden thinks that strychnine, phostigmine, and pilocarpine increase the tone of the atonic stomach. He has seen no benefit derived from wearing abdominal binders as regards the position of the stomach, which he determined by the Röntgen rays. However, a binder frequently adds to the general comfort of the patient and is of use especially in nervous patients.

**The Treatment of Gastric Disease with Aluminum Silicate.**—ROSENHEIM and EHRMANN (*Deutsch. med. Woch.*, 1910, iii, 111) report their observations regarding the action of aluminum silicate in gastric affections especially those dependent upon a stimulated secretion. They say that in all cases of hyperacidity or hypersecretion of neurotic origin, or associated with organic disease, aluminum silicate acts most favorably in reducing the acidity, quieting the pain, and aiding digestion. Aluminum silicate, as prepared by Kahlbaum under the name neutralon, is a fine, tasteless, and odorless powder insoluble in water. An ideal remedy, they say, should have the power to bind the excessive hydrochloric acid in a harmless combination, and also should have a protective and an astringent effect upon the mucous membrane. They claim that aluminum silicate has these advantages. When taken into the stomach it is broken up by the hydrochloric acid forming silicic acid and aluminum chloride. They state that aluminum chloride has a protective and astringent effect upon the gastric mucous membrane similar to that of silver nitrate and bismuth, without the disadvantage of a possible toxic action. Furthermore, silver nitrate at times causes diarrhoea, and bismuth is constipating. They gave aluminum silicate

in doses of from one-half to one teaspoonful in about three ounces of water one-half to one hour before meals. There were no untoward symptoms from its use. Theoretically they attribute an intestinal antiseptic action to the aluminum chloride and are endeavoring to determine this by further observations.

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**Substitutes for Digitalis.**—MENDEL (*Med. Klin.*, 1909, xli, 1551) says that the full benefit of digitalis can only be obtained from preparations containing the mixed glucosides of digitalis. Since the mixed glucosides are responsible for the gastro-intestinal irritation, the only sure way we have of avoiding them is to give the drug intravenously. Digitalin, digitoxin, and digalen do not contain the mixed glucosides, and consequently Mendel has given up their use. He speaks very highly of digitalone, which is prepared from the fresh leaves and accurately standardized. Mendel has given digitalone to more than 200 patients, and has never seen any cumulative action or other untoward effects. The effect of a single dose is not so marked as that of digalen or strophanthin, but Mendel believes it is infinitely safer. Strophanthin and digalen are dangerous because of the tendency to an overstimulation, with consequent depression of the heart. Mendel has seen a large number of patients with marked cardiac insufficiency, who because of their inability to take digitalis internally were kept alive for years by the intravenous use of digitalone. Furthermore, he has found that a single injection of digitalone was often sufficient in cases of acute cardiac failure.

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**The Treatment of Acute Pulmonary Œdema.**—MILLER and MATTHEWS (*Arch. Int. Med.*, 1909, iv, 356) base their article upon an experimental research on acute pulmonary œdema. They state that a knowledge of the causes producing an œdema is essential to its treatment. Pulmonary œdema is usually a manifestation of some circulatory disturbance. This circulatory disturbance may be due to high blood pressure. In such a case drugs that increase arterial tension are harmful, and so are contra-indicated. The blood pressure should be reduced by bleeding, by counterirritation to the surface of the body, or by drugs that lower the blood pressure. On the other hand, the type of œdema associated with low blood pressure should be treated by drugs raising the blood pressure. They advise against the use of atropine in pulmonary œdema associated with high arterial tension. Atropine is frequently recommended in pulmonary œdema based on its power to lessen secretions. However, the œdema is not due to an increase of secretion, but to a transudation. They believe that adrenalin is probably never useful and often may be dangerous. The inhalation of oxygen is harmless, and often gives temporary relief. Morphine is decidedly beneficial in any type of pulmonary œdema relieving the nervous apprehensions of the patient.

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**Choral Hydrate as a Local Application.**—HELLER (*Münch. med. Woch.*, 1909, xlvii, 2418) has used chloral hydrate as a local application in various inflammatory conditions of mucous membranes. He employs a 2 per cent. solution of chloral hydrate in the form of a spray in the treatment of acute tonsillitis. Chloral hydrate has both antiseptic and

anesthetic properties, and is especially useful to relieve pain. He found it of value in the treatment of diphtheria, Vincent's angina, syphylitic ulcerations, and ulcerative stomatitis. When the secretions are foul smelling, chloral hydrate also acts as a deodorant.

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## PEDIATRICS.

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UNDER THE CHARGE OF

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**Unusual Persistence in the Secretion of Colostrum.**—H. MERRIMAN STEELE (*Archiv. Pediat.*, 1910, xxvii, 32) reports the following case of persistence of the colostrum in a healthy young woman nursing her first child. The baby weighed seven pounds and five ounces at birth and was normal in every respect. It lost steadily in weight, and when it was two weeks old weighed six pounds four ounces. It nursed regularly, seemed satisfied, and had no vomiting or regurgitation. The stools, at first normal, now became greenish and contained some mucus and fatty and proteid curds. There was no fever, and the child slept well. There was scalding about the buttocks, and seborrhœic eczema developed about the face and chest. The mother had a normal convalescence, and her milk was abundant, rich, yellow, and thick. A sample taken for analysis, after standing on ice for ten hours, showed a thick layer of cream resembling butter, the whole specimen being a deep yellow with an olive tint. Analysis showed fat, 3.60 per cent.; proteids, 1.70 per cent.; specific gravity, 1030. As this was not far from normal and the color was peculiar colostrum was suspected. A specimen placed under the microscope showed typical colostrum. The majority of the corpuscles were colostrum bodies and the fat globules varied from minute to exceptionally large size. The baby was taken from the breast and given castor oil. It was weaned on partially peptonized cow's milk and gained four pounds twelve ounces in nine weeks. The skin cleared in eight days. Colostrum continued to be secreted for three weeks, the last examination showing precisely the same condition. In total, the colostrum was secreted thirty-two days, it being fairly assumed that the secretion was colostrum up to the first examination.

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**Dried Milk as a Food for Infants.**—C. K. MILLARD (*Brit. Med. Jour.*, 1910, i, 253) describes the preparation and use of dried milk and the results obtained from its use as an infants' food. Dried milk is prepared by feeding fresh milk in a continuous stream on to revolving cylinders heated by steam to about 250° F., the moisture in the milk being instantly dispelled. A thin film of dry milk forms on the cylinder and is detached by knife-edges. It is subsequently passed through a sieve and is obtained as a coarse, granular, cream-colored powder practically sterile, which, in air-tight packages, will keep almost in-



definitely. The relative proportions of the main constituents—proteids, fats, milk sugar, and salts—remain practically unchanged, but changes occur in the more complex albuminoids and enzymes, similar to those in boiled milk. The extremely short time during which the milk is subjected to the heat by the Just-Hatmaker process described above, may cause less change than occurs in boiling. When mixed with water, about 60 per cent. of the dried milk is soluble, the remainder is readily suspended. This dried milk has been used at an Infants' Milk Depot for eighteen months, for about two hundred infants. One advantage discovered was greater digestibility; many infants with whom liquid milk did not agree, thriving on the dried form, and retained it. This difference is accounted for by the character of the curd formed in the stomach which does not tend to form hard cheese-like masses. All infants not thriving on bottled milk were placed on the dried milk, with excellent results. After a period of ten months or longer careful records and investigations showed no scurvy or rickets resulting from its use and no bad after-effects have been discovered. The advantages of the dried milk appear to be: *Ease of digestion*, *bacterial purity*—freedom from tubercle bacilli and contamination by flies. *Conservatibility*—no "souring" in hot weather. *Convenience*—a definite quantity being mixed with warm boiled water. *Cheapness*. The presumed destruction of the antiscorbutic properties of the milk is theoretical, but can be compensated for, if thought necessary, by administering fruit juice. Dried milk, being after all "only milk," is in an entirely different category from all patent foods prepared from cereals, and is superior to them.

#### **Cyclic or Recurrent Vomiting with Hypertrophic Stenosis of the Pylorus.—**

A. E. RUSSELL (*Brit. Jour. Children's Dis.*, 1910, vii, 49) supports the argument that muscular spasm of the pylorus due to hypertrophic stenosis is sometimes the cause of cyclic vomiting with its attendant conditions. He cites as an example the case of a boy, aged four years, and nine months, who from birth was subject every few months to attacks of vomiting with epigastric pain. The attacks appeared suddenly and lasted twenty-four hours, the vomiting recurring during the day. The child's last illness began with an attack lasting one week, during which the vomitus turned from yellow to coffee color. There was great prostration, emaciation, and the breath smelled strongly of acetone. There was constipation and the urine contained acetone and diacetic acid. Then a period of remission occurred lasting nineteen days, during which the child ceased vomiting, took nourishment and improved. The urine became free of acetone and diacetic acid. There was then a return of the vomiting and epigastric pain and after five days the child died, acetone and diacetic acid again having appeared in the urine. The autopsy showed a considerably dilated stomach. The lumen of the pylorus was very small and its walls were thickened. There was no ulcer or scar tissue present and the remaining thoracic and abdominal organs were normal. These symptoms are practically identical with those of cyclic or periodic vomiting in children. The current views as to cyclic vomiting are that it is due to a poisoning arising from the intestinal tract, with imperfect oxidation of fats and an accumulation of them in the liver. Russell argues that acute starvation accompanies this condition, as evidenced by the emaciation and the

acetone bodies in the breath and urine (with the fatty changes in the liver often found in these cases). He claims that these latter conditions can be explained by the acute starvation involved with cyclic vomiting, and that the cause of the vomiting is elsewhere, probably in the hypertrophic stenosis of the pylorus. While actual stenosis of the pylorus is not an essential factor in the disease, he submits that the attacks were due to the occurrence of pyloric spasm. On this hypothesis, as long as pyloric spasm lasted obstruction would be complete. If it persisted long enough, acute starvation would necessarily follow with the resulting acidosis. Fatal issue followed on the inanition and exhaustion. While possibly not a factor in all cases, pyloric spasm is enough to account for recurrent attacks of vomiting and presents all features described as characteristic. It is also consistent with the fact that the attack often comes on suddenly. Relaxation of the spasm would be followed by this sudden cessation of the attack, which is often a noticeable feature.

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**An Epidemic of Acute Poliomyelitis.**—W. W. TREVES (*Brain*, 1909, xxxii, 28) records the occurrence of an epidemic of 8 cases of acute anterior poliomyelitis in Upminster, a town of 1700 inhabitants. It was the first epidemic of its kind in the town, and no case of infantile paralysis had occurred there in several years. The months of the epidemic were hot and dry, but the heat was not excessive. Six of the patients had constitutional symptoms and a few days afterward were paralyzed; one child had fever, but developed no paralysis; the eighth was paralyzed without any constitutional symptoms. The legs were the members most commonly affected. In some of the children the eyes attracted the parents' attention by their peculiar look, but in no case was any definite evidence of polio-encephalitis obtained. Seven of the children were over six years of age, one was three and one-half. In 5 of the cases the period of incubation could not have been more than six days. All attempts to trace the means by which the disease spread failed. Of 32 other epidemics recorded in literature and discussed by the author, but 2 occurred in England.

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**The Dwarf Tapeworm, an Intestinal Parasite in Children.**—OSCAR M. SCHLOSS (*Archiv. Pediat.*, 1910, xxvii) reports 14 cases of dwarf tapeworm or *Hymenolepis nana*, in 230 children. The average length of the worm is from 14 to 16 mm. The distal half is broad, while the proximal half becomes narrow. The segments are from 3 to 6 times as broad as long and the head of the worm is globular and carries four suckers and a rostellum armed with twenty or thirty bifid hooklets. Its habitat in man is in the upper two-thirds of the ileum. The eggs are slightly oval and have two membranes widely spaced. From the poles of the inner membrane are projections from which spring filaments which ramify in the space between the membranes. This is characteristic. The 230 children examined were from the tenement-house district, and, with one exception, were all born in New York City. Six of the 14 cases observed showed no symptoms referable to the parasite. The remaining 8 cases showed gastro-intestinal and nervous symptoms. Under the former, epigastric pain, nausea, vomiting, and an increased appetite were prominent. Restlessness at

night, grinding the teeth, itching of the nose, and genital pruritus under the latter. Eosinophilia was present in 7 of the 8 cases suffering from symptoms of the parasite. In cases with no symptoms eosinophilia was uniformly absent. A secondary anemia was generally present. The absence of, and variety in, symptoms are probably due to the site of mechanical irritation in the intestine and to toxic effects. The mode of infection is through ingestion of the ova in food. No intermediate host has been found in any human food. The dwarf tapeworm, however, has frequently been found in the small intestine of rats. Auto-infection is possible, owing to the great number of ova in the feces. The diagnosis is made by finding the characteristic ova in the feces or by obtaining the parasite after treatment. The treatment consists of a preliminary period of two or three days on liquid diet, a preliminary purge and the administration of oleoresin of male fern in mixture, emulsion, or capsule. The dose for a child two to four years old is 0.5 dram; four to six years, 40 grains; and six to twelve years, 1 dram. This is given on an empty stomach. It is divided into three or five doses and given at half-hour intervals. A brisk cathartic is given a half an hour after the last dose is taken. When the treatment is not effective the ova reappear in the feces in fifteen days.

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## OBSTETRICS.

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UNDER THE CHARGE OF

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**The Diagnosis of Puerperal Septic Infection.**—SACHS (*Zent. f. Gynäk.*, No. 46, 1909) gives the result of 200 examinations of lochial discharge and blood in septic cases. This study was made to determine the significance of hemolytic streptococci in the blood as well as in the lochial discharges. He agrees with Veit that serious puerperal septic infection is caused by these organisms, which are present in the great majority of cases. By using fluid blood agar media he was able to recognize hemolytic streptococci in two-thirds of the cases. It is not sufficient to recognize a few of these organisms to make a diagnosis of infection. Their presence must be sought in the blood and their frequency estimated. When puerperal ulcers with hemolytic streptococci are present the prognosis is better than if peritonitis has developed. Recognition of hemolytic streptococci in healthy puerperal patients has absolutely no significance with regard to their importance in cases of sepsis. When these germs are not found in a septic patient, the prognosis is good. As an exception to this, are those cases late in the puerperal period in which hemolytic streptococci have passed from the uterus and have caused suppuration in thrombosed veins, and are no longer recognized in the secretion of the uterus; also in cases of sinus thrombosis and other intercurrent affections in which the streptococcus is the active agent.

In cases of mild infection in greatly weakened persons after severe hemorrhage or asphyxia following anesthesia, a fatal result may follow, although hemolytic streptococci are not found. When peritonitis develops early in the puerperal period perforation of the uterus must be suspected, and in these cases hemolytic streptococci might not be obtained from the uterine cavity. The mortality statistics of surgical operations in streptococcic peritonitis give 50 per cent. recoveries, and 50 per cent. deaths. This favorable showing is to be explained by the diminished virulence of the germ, and the fact that many of these cases are perforation of the uterus. The high mortality of severe puerperal sepsis arises in great part from the fact that a differential diagnosis between the mild and severe cases is not made sufficiently early to be of use in the treatment. Clinical observation will often determine the degree of severity in septic infection, but bacteriological examination is a most useful adjunct.

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**Modification of Peripheral Sensation during Pregnancy.**—PONDOLFI (*Annali di Ostetricia et Ginecologia*, No. 9, 1909) contributes a paper upon this subject, describing an apparatus which he has devised for testing the peripheral sensibility of patients during pregnancy. His experiments were made upon the fingers, and in all 30 cases were studied. He concludes that peripheral sensibility to pain during gestation is very considerably decreased.

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**Ovariectomy and Myomectomy Early in Pregnancy, with Full Term Delivery.**—GRAD (*Jour. Amer. Med. Assoc.*, November 27, 1909) reports the case of a patient in her first pregnancy brought to the hospital because she had fainted on the street, after complaining of sudden abdominal pain, with vomiting and collapse. This pain gradually subsided, leaving the abdomen tender. There was a history of cramp-like pain in the abdomen, with moderate fever, indigestion, and disturbance of the bladder, for a week or ten days prior to this attack. The patient had been married nine years, but had not previously been pregnant. On examination the uterus was slightly enlarged, with several fibroid nodules. A large movable tumor was also detected in the pelvis. The diagnosis of ovarian cyst with twisted pedicle and pregnancy in a fibroid uterus was made. At operation the pedicle of the cyst was ligated and the tumor removed. Three fibroids were enucleated without especial difficulty. Although the patient had a bloody discharge from the uterus after the operation, the ovum was retained, and the patient went to term and was subsequently delivered by the use of forceps.

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**Ovarian Cyst with Twisted Pedicle Complicating Pregnancy.**—RUSHMORE (*Surg., Gynecol., and Obstet.*, November, 1909) reports the case of a multipara, who on the day before her admission to the hospital had cramp-like pain low down on the left side. Examination under chloroform revealed pregnancy with an ovarian tumor. On opening the abdomen an ovarian cyst on the left side with the pedicle twisted one and a half times, dark purple, almost black in color, was found. The tissue was very soft and friable, and the wall of the uterus bled freely. The tumor was successfully removed, and the mother made a good recovery,

a healthy child being born at full term. On examination the tumor was a dermoid cyst of the ovary with strangulated pedicle and a partial strangulation of the Fallopian tube. The article concludes with a review of the literature of the subject.

**Artificial Reproduction of the Amniotic Liquid during Labor.**—SCHALLEHN (*Archiv f. Gynäk.*, 1909, lxxxix, Heft 2) reports five cases of premature escape of the amniotic liquid, in which Bauer's elastic bag was introduced, distended with salt solution, and allowed to remain in place in the membranes. In several cases in which the heart sounds had become weakened through birth pressure they improved after the bag was introduced. If the patient suffered much pain from pressure, morphine was given hypodermically, and the patient was delivered so soon as the cervix was dilated by version or forceps. The presence of the bag seemed to excite uterine contractions and lessen the risk of fatal birth pressure for the child. It was used in these cases, not primarily to dilate the cervix, but to protect the child from pressure; secondarily to soften the cervix and expedite labor.

**The Results of Pregnancy Occurring After Operations for the Correction of Retroflexion.**—BIRNBAUM (*Archiv f. Gynäk.*, 1909, lxxxix, Heft 2) reports the results in 20 cases operated upon for retroflexion by ventrofixation. In 4 of these pregnancy occurred, terminating in labor without complications. In these cases there were evidences of peritoneal adhesions and alterations of the tubes and ovaries. These were detected at the operation. The cause of the sterility which had existed before operation seemed to be the kinking in the Fallopian tubes, which was caused by the retroflexed condition of the uterus. In 3 cases no cause could be found at operation for the peritoneal adhesions; in 1 case a previous parametritis had undoubtedly existed. In the 16 other cases in which operation was done for retroflexion, pregnancy had not occurred at the time of writing. It is questionable whether lesions indirectly produced by the retroflexion were not responsible for the sterility in these cases.

## GYNECOLOGY.

UNDER THE CHARGE OF

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**An Ovarian Abscess Containing a Lumbricoid Worm.**—FRY (*Jour. Amer. Med. Assoc.*, 1909, liii, 1028) reports a case of ovarian abscess that contained a lumbricoid worm. The patient was twenty-three years of age. The right appendage was inflamed and adherent. The left ovary and tube were adherent to the uterine cornu. The ovary was enlarged to the size of a hen's egg, the surface smooth and

non-adherent to intestine. It ruptured during removal and 30 c.c. of pus escaped into the abdominal cavity. Projecting from the abscess through the rupture was a lumbricoid worm 6 or 7 cm. in length. It was dead and flattened. The worm was identified by Dr. B. H. Ransom of the United States Department of Agriculture. The pus contained *Bacillus coli communis* in pure culture. Fry concluded the worm had gained access to the ovary by the vaginal route and entered the ovary through a ruptured Graafian follicle.

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**The Choice of Operations for Retrodisplacements of the Uterus.**—BENJAMIN (*Jour. Amer. Med. Assoc.*, 1909, liii, 1072) states: Retrodisplacements of the uterus often cause much discomfort. The harmonious action of all the supports is essential to the uterus for its normal position. The operation which interferes with the laws governing the normally placed uterus is not to be advocated. The operation which produces unnecessary intra-abdominal traumatism should not be chosen in the ordinary case. Operations which could possibly interfere with the enlargement of the uterus during pregnancy should be used in selected cases only. Operations which leave an additional suture line within the abdomen may cause subsequent trouble. Operations which do not give as strong a support as possible consistent with the normal functions of the uterus may result in failure in some cases. The operation which utilizes the normal ligaments with little or no traumatism is less troublesome and more scientific. Benjamin then describes his modification of Gilliam's operation for shortening the round ligaments and gives the advantages of it.

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**The Endometrium and Some of its Variations.**—GARDNER and NOVAK (*Jour. Amer. Med. Assoc.*, 1909, liii, 1155) deprecate the employment of many terms in quite common use, that are now known to have been coined from mistakes in pathology. They believe Hitschmann and Adler have taken an extreme view in practically asserting that glandular changes do not occur except in connection with the menstrual process. Both animal experimentation and clinical observation indicate that the actual underlying cause of menstruation is the secretory activity of the ovary, which produces an internal secretion or hormone essential for its occurrence. The principal effort of this substance seems to be of a vasomotor nature, and is exerted especially on the pelvic bloodvessels. It is only natural to suppose that the endometrium plays a purely passive role in this phenomenon, and that the histological changes observed in connection with menstruation represent merely the reaction of the endometrium to the process—a reaction which may, however, be elicited by influences other than that of normal menstruation.

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**Factors which Contribute to a Reduction in Mortality in Abdominal Surgery.**—F. F. SIMPSON (*Jour. Amer. Med. Assoc.*, 1909, liii, 1173) discusses in detail the factors contributing to a minimum mortality rate in abdominal surgery. While it is a paper not amenable to being satisfactorily abstracted, his conclusions may be considered as follows: An accurate knowledge of the nature, extent, and kind of disease, and exact determination of the patient's margin of reserve strength; a judicious adaptation of the time and type of operation to

individual needs; a group of competent operative co-workers; a minimum amount of anesthetic; a rigid aseptic technique; and speed with precision, are factors which will yield a low mortality and highly satisfactory operative results.

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**The Age of Menstruation in Egyptian Girls.**—MRS. B. SHELDON ELGOOD, Assistant Medical Officer, Ministry of Public Instruction, Cairo (*Jour. Obst. and Gyn. of Brit. Emp.*, 1909, xvi, 242) has studied the subject of the date of first menstruation in Egyptian girls, her field of inquiry being several large schools for native Egyptian girls. In 83 menstruating girls, the birth certificates of whom were available, she found the first appearance of menstruation in 12 was at twelve years; in 44, at thirteen years; in 21, at fourteen years; and in 4, at fifteen years. This study tends to prove that at thirteen and fourteen years 80 per cent. of native Egyptian girls begin to menstruate.

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**The Anatomy of Tubal Convolutions and the Mechanism of Tubal Occlusion.**—JAMES YOUNG (*Jour. Obst. and Gyn. Brit. Emp.*, 1909, xvi, 307) states that his analysis of the various theories advanced to explain the disappearance of the tubal fimbriæ reveals the fact that they fall under one or other of two headings: (1) The first class includes the theories, which explain the process as being due to an increase in the total length of the tube wall, which, by expanding in an outward direction, becomes projected beyond the tubal fimbriæ. According to the theory of Alban Doran, which receives the support of Kleinhans, the increase in length is dependent on the swelling and increase in substance of the tube wall associated with salpingitis, etc. According to Emil Ries the gliding outward of the "peritoneal ring" over the fimbriæ is rendered possible by the fact that the walls become loose and redundant subsequent to the collapse of a distended tube. (2) In the second category are included the theory of Opitz, which explains the process as due to retraction of the muscular and mucous coats of the tube within the serous coat, and the theory described in this paper, in which the gliding process involves only the mucosa and inner coat of muscle. In the so-called "perimetritic closure" of Alban Doran the sealing of the opening is explained by a matting together of the fimbriæ by inflammatory adhesions without a preliminary recession.

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**Removal of an Unusually Large Ovarian Tumor.**—KNIGHT (*Amer. Jour. Obst.*, 1909, lxi, 441) reports the successful removal by abdominal section of an ovarian cyst weighing one hundred and eleven pounds. It had been observed for ten years by the patient and was removed without preliminary aspiration.

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**Enucleation of Uterine Myomas; Why and When Performed.**—MONTGOMERY (*Jour. Amer. Med. Assoc.*, 1909, liii, 1245) suggests the following conditions as indicating hysteromyomectomy: (1) When the growths are few in number and the structure of the uterus is but little involved. Of course, the fibroids may be numerous but situated so near the surface as to permit their removal with but little injury to the general structure, but the large number indicates a tendency to fibroid degeneration which presages early redevelopment. When a number

of growths of considerable size are present, the structure of the uterus is so spread out and will be so injured as to render an attempt to save the organ attended with danger during the subsequent convalescence and an element of danger in the event of pregnancy and labor. (2) When the growths are readily accessible through the vagina or cervical canal. A growth within the uterus, either a sessile, submucous, or an interstitial, is readily attacked. Not infrequently, the canal may be partially dilated and the dilatation can be completed by the introduction of tents, or the cervix may be split bilaterally until the tumor is exposed or rendered accessible. The enucleation completed, the cavity may be packed with gauze and the split cervix closed much as is done in an ordinary trachelorrhaphy. The vaginal operations are attended with less constitutional disturbances than in the removal by an abdominal incision. (3) When the woman, whether unmarried or married, is under forty years of age, and particularly when she is childless or has but one or two children. The removal of the growths at an earlier period cannot be considered as rendering certain the escape of the patient from recurrence, for one of his patients who had two fibroids enucleated when she was thirty-three years old, five years later had twenty removed. The age of forty, however, is one at which the individual suffering from such growths begins to undergo retrogressive degenerations, and when the patient has not previously been fertile pregnancy is much less likely to occur. (4) When the tubes and ovaries are free from complicating conditions. The existence of tubal or ovarian disease of sufficient gravity (as hydrosalpinx, or pyosalpinx, or ovarian hematoma), to render the probability of conception remote or to necessitate the removal of tubes and ovaries to insure restoration of health, should also be an indication for the removal of the fibromyomatous uterus. While it is true that in the majority of cases the tumors decrease and become quiescent after the menopause, yet they sufficiently often undergo necrosis and other degenerative changes to justify the removal of the uterus.

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## OPHTHALMOLOGY.

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**Treatment of Detachment of the Retina.**—DEUTSCHMANN (*Ophthalmoscope*, November, 1909, p. 737), in demonstrating his methods of operating for this condition, bisection and injection of the sterile vitreous humor, formulates the following rules: Bisection: never operate upon a recent detachment so long as the detached part is situated in the upper part of the fundus; the bisection is to be made with a double-edged linear knife downward in the anterior boundary of the cul-de-sac.



Bisect horizontally, guide the knife tangentially to the eyeball from downward and outward to downward and inward. Make the bisection as quickly as possible in a straight direction through the eyeball avoiding the junction at the spot of the counter puncture, and draw back the knife in the same way it was introduced. Turn the blade a little at the spot of the puncture, so that the retinal and eventually the preretinal fluid can escape. The operation can be repeated twenty times or oftener unless interference has been followed by any unfavorable result. Bandages should be applied to both eyes for the first twenty-four hours and then only upon the operated one for four or five days. Atropine should be employed during the entire treatment and the patient kept in bed for a week after each operation. The injection method is reserved for cases otherwise hopeless.

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**Myopia and Light Sense.**—LANDOLT (*Klin. Monatsbl. f. Augenhk.*, October, 1909, p. 369) concludes that the light sense is not influenced in myopia even of high degree unless decided chorioretinal changes are present, and even the latter do not always diminish that function; neither does astigmatism have any effect, and light sense and visual acuity are independent of each other. Age, however, appears to diminish the faculty in myopes as well as in emmetropes and hyperopes.

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**Report upon 103 Cases of Magnet Extractions.**—HAUSMANN (*Klin. Monatsbl. f. Augenhk.*, 1910, xlvii, 86) reports that of 103 magnet extractions from the ophthalmic clinic of the University of Halle, the vision ranged from  $\frac{5}{8}$  to  $\frac{5}{15}$  in 37 cases; from  $\frac{1}{3}$  to  $\frac{1}{80}$  in 11 cases; and less than  $\frac{1}{80}$  in the same number; in 15 cases the form of the eyeball was maintained, though the vision was lost; in 7 there was phthisis bulbi, and in 22 enucleation or evisceration had to be performed.

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**Etiology of Subacute and Tardy Infection Following Operations.**—(Ophthalmic Section of XVIth International Congress of Medicine, Budapest, *La Clin. Ophthal.*, November 10, 1909, p. 567). Following a lengthy discussion upon the infectious complications which sometimes follow iridectomy, extraction of cataract, discission, sclerotomy, and other operations upon the cornea, iris, uveal tract, or vitreous body, MORAX comes to the following conclusions: The tardy appearance of an iridociliary infection of subacute development can be provoked by a late development of pyogenic microbes, which have been introduced at the time of the operation. Although bacteriological examinations are still liable to be misinterpreted and while the explanation of the majority of such cases of iridocyclitis is purely hypothetical, the reporter is inclined to believe that they are in general due to the development of little known saprophytes and still undescribed spores which have their seat upon the surface of the conjunctiva of certain individuals. These germs offer to the usual methods of disinfection of the conjunctival cul-de-sac greater resistance than the ordinary pyogenic microbes. At the same session Angelucci considered postoperative inflammations caused by auto-infection. Senile and arthritic albuminuria occasion no interference with the cicatrization of wounds; grave forms of Bright's disease, however, frequently give rise to iritis. Neither does diabetes, save in its graver forms, interfere with the healing process. Gout

introduces no complications except when there is also disturbance of the intestinal tract. Postoperative iritis frequently appears in connection with dental suppuration, constipation or intestinal infection, and occasionally also in vesical catarrhs. Influenza may provoke endogenous suppuration in an eye recently operated upon, and so may furunculosis and abscesses, no matter where situated.

**Nervous Asthenopia from Electric Light; Use of Yellow Glasses.**—DE WAELE (*Archiv. d'Ophthal.*, September, 1909, p. 566) publishes six instances in young persons in whom asthenopia was produced by working under arc lights. While the electric light may be no richer in ultra-violet rays than solar light, the former is more dangerous because the eye is more directly exposed. Electric lights should be provided with glass globes (yellow is the best), or at least so placed or screened that the eyes shall be protected from the direct rays. When this can not be done yellow glasses should be worn.

**Trachoma in the Abruzzi, Italy.**—GUISEPPE'S (XIth International Congress of Ophthalmology, *Rec. d'Ophthal.*, August, 1909, p. 255) statistics show what ravages trachoma causes in that country; in a population of 147,000, more than 2000 cases of trachoma are known. The disease is especially common in the valleys, the mountains being almost exempt. In many communities the malady has been imported by Italian emigrants returning from Brazil.

**Subcutaneous Injections of Alcohol in Blepharospasm and Spastic Entropion.**—FUMAGALLI (*Annali di Oftal.*, 1909, xxviii, fasc. 3, p. 162), at the Clinic of Turin, makes the injections superficially in the neighborhood of the stylomastoid foramen under the skin, in the region of the supra-orbital nerve and of its palpebral filaments and in the distribution of the orbital filaments of the facial so as to affect the orbicularis. Thirty parts of absolute alcohol and 60 of sterilized water is the injection employed without an anesthetic. A syringe of Pravaz is used for the supra-orbital region, and in inveterate cases of essential blepharospasm a similar quantity is employed for the infra-orbital region. A single injection under the skin of the lid, in the centre and parallel to the free border, suffices in spasmodic entropion (children and the aged). Several injections may be made daily or at longer intervals until cure or considerable amelioration is obtained.

**Helmholtz's Theory of Accommodation.**—ROCHE (*Rec. d'Ophthal.*, October, 1909, p. 325) observed a case of complete bilateral ectopia of the lens. The aphakic portion of the pupil was hyperopic 10 D.; the portion opposite the lens was myopic 13 D. This case and others like it furnish a conclusive argument in favor of Helmholtz's view that during accommodation the zonula is relaxed, against the opinion of Tscherning that the act of accommodation is brought about by tension of that membrane. The fact that increase of the refraction is not always observed in luxation of the lens may be due to the circumstance that the fibers of the zonula are not completely torn through—there is subluxation, a comparatively small number of fibers being sufficient to maintain the shape of the lens.

## PATHOLOGY AND BACTERIOLOGY.

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UNDER THE CHARGE OF

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**The Nature of Antitrypsin in the Blood Serum and its Mode of Action.**—Piek and Pribram have shown that when the blood serum is treated with ether it is robbed entirely of its antitryptic qualities. This naturally suggests that the antifermentive property of the serum is in some way dependent upon the presence of lipoid substances. O. SCHWARZ (*Wien. klin. Woch.*, 1909, xxii, 1151) has reported and confirmed these experiments, and in investigating the subject still further brings out many points of interest. He has found that 5 per cent. emulsion of lipoid will inhibit, though not as powerfully as the same quantity of blood serum, the proteolytic action of trypsin. Blood serum which has been inactivated by extraction with ether may be re-activated again by the addition of amounts of lipoid emulsion, not in themselves markedly antitryptic. The re-activation does not take place, however, unless the lipoid and serum are allowed to remain in contact for one hour at 65° C. It seems, therefore probable that the lipoids must form a combination with albuminous substances of the serum in order to assume an antitryptic power. It could further be shown that when this albumin-lipoid complex is brought in contact with a solution of trypsin a portion of the trypsin is actually used up and is probably bound to the inhibiting substance. As far as could be learned the antitryptic and antipeptic properties of the serum are not identical, for when the serum was inactivated by ether extraction for trypsin it was still active against pepsin. Finally, in a few isolated experiments, it could be shown that the antitryptic property of the serum increased in proportion to the amount of lipoids present. Many observations have been made upon the antitryptic and antileukoproteolytic power of the serum in various diseases, and this property has been found to vary widely, but a number of observations seem to show that an increase in the antitryptic and antileukoproteolytic property accompanies an increase in the number of white cells. This Schwarz believes is due to the destruction of cells with subsequent liberation of lipoids and not, as has been suggested, to the formation of a true antiferment in the sense of an antibody, through the liberation of ferment substances in the blood.

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**The Venous Pulse under Normal and Pathological Conditions.**—RUBIN (*Zeit. f. Exp. Path. und Ther.*, 1909, vi, 619) discusses extensively from an experimental point of view the mechanism of the venous pulse, and his work must be the final word on a number of points. In his experiments 133 dogs were used, and observations were made with the

thorax both opened and closed. He found that the placing of a funnel over the pulsating parts gave more delicate results than when a manometer was used. The three principal venous waves, the *a*, the *c*, and the *v* waves are discussed separately. Rihl concludes that the *a* wave is caused entirely by the auricular systole. An actual column of blood is sent up into the vein by the auricle and the pressure of this column carries the wave above the intact vein valves. It is not a passive or congestive wave. The *a* wave is increased by increase of auricular systole, auricle and ventricle contracting simultaneously, and by venous engorgement. The latter cause may increase the wave even when the auricular systole decreases. The *a* wave is diminished by a decrease of auricular systole, and from this cause it may disappear. The ventricular activity causes two venous waves, the *c* wave and the *v* wave. These occur when the ventricle contracts without the auricle. The *c* wave is not dependent on the motion of the aorta or carotid artery. The *c* wave and the carotid pulse are synchronous when funnels are used on both sides, and the *c* wave, which follows a little after the systolic contraction, is not effected by the presence or absence of the auricular systole. When the venous wave is taken from a deeply inserted cannula in the heart the *c* wave is synchronous with the ventricular systole. The relation between the *a* wave and *c* wave depends, in part, on the time between the *a* and *v* systole, but is also dependent on the size of the *a* wave. Too much dependence should not, therefore, be put in this relation in determining the state of the conduction of the heart beat. The *v* wave commences during ventricular systole, and this fact shows that it is not dependent on ventricular diastole for its formation. This wave is best considered as formed by two forces, the engorgement of the vein during ventricular systole, and the movement of the base of the heart upward at the beginning of diastole. When a division occurs in the *v* wave corresponding to the point where the two forces meet, it is synchronous with the diastolic notch, as seen in the carotid artery tracing. This division represents, therefore, the opening of the atrioventricular valves. This *v* wave is increased and decreased with the increase and decrease of venous engorgement. Slight tricuspid lesions cause no changes in the *v* wave, but grave lesions increase it and make it come earlier in systole. Only with the highest grade lesions does the ventricular type of venous pulse occur.

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**The Cause of Arteriosclerosis.**—HARVEY (*Virch. Archiv*, 1909, cxvi, 303), attempting to discover what part increased blood pressure might play in the production of arteriosclerosis, has compressed the abdominal aorta of young rabbits for three minute periods over a prolonged time. By actual manometric tracing it was found that digital compression of the aorta in rabbits raises the blood pressure at times 42 mm. It was found that by this method extensive sclerosis could be produced in the aorta above the point of compression. The sclerosis was of the type described by Monkeberg in man, and consisted in degeneration of the muscular coat with deposits of lime salts. Harvey believes that the sclerosis produced in rabbits by injection of adrenalin, nicotine, etc., is caused not by a toxic action of the drugs, but by their power to increase blood pressure.

**Changes in the Chromaffin System in Cases of Unexplained Postoperative Death.**—JOSEPH HORNOWSKI (*Virchow's Archiv*, 1909, cxcviii, 98) points out that sudden death after operation, with symptoms of shock, has been explained by hypotheses only—*e. g.*, chloroform, heart failure, etc. He argues however, that this is not correct and that such definite clinical symptoms as these cases present must have an equally definite cause. This cause he attempts to show lies in the so-called "phaochrome" or chromaffin cells of the adrenal glands and sympathetic ganglia, and brings forward as an analogy the extreme asthenia of Addison's disease in which these cells show marked change. This change is a loss of brown color when stained by chrome salts. In four cases of death shortly after operation he found the phaeochrome cells of the adrenals and sympathetic ganglia either colorless or only very faintly yellow. From these and other unreported observations Hornowski concludes that the pale appearance of these cells is the sign of a lack of activity on their part, or a lack of the "pressure-maintaining substance" which they produce and is, therefore, sufficient to explain death in the absence of other causes. With this hypothesis as a starting point the author reasons that the blood-pressure-lowering effect of chloroform is offset by the secretions of the chromaffin cells. This extra call upon the cells tends to exhaust them, but in addition the drug exerts a toxic action upon them, so that a point is reached where the cells are no longer able to meet the vital demand and death ensues. As suggestive corroborative clinical observations the author mentions the occurrence of death in those cases in which the patient passes through a long period of excitation in the first stages of anesthesia and consequently uses a greater amount of the "pressure-maintaining substance." Furthermore he cites those patients that feel unduly well and bright immediately after operation and then go on to sudden death. This stimulated condition he believes is a manifestation of excessive production of the substance, and the rapid subsequent collapse evidence of exhaustion of the chromaffin cells. Hornowski then undertook animal experiments. He anesthetized rabbits for various lengths of time and also injured the sympathetic ganglia. He found that short deep chloroforming produced no change in the phaeochrome cells. Repeated, long chloroforming, however, caused the cells to fail to take the chrome stain. Trauma, on the other hand, to the peritoneum, adrenals, and sympathetics, produced rapid loss of color in the cells of the chromaffin system. The author concludes that the brown color (chrome reaction) is an indication of the power of the cells to produce the "pressure-maintaining substance," and that if the organism can meet the increased demand for this substance caused by chloroform and trauma—in the face of the toxic effect of the chloroform—death does not occur.

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ORIGINAL ARTICLES.

THE TREATMENT OF INTESTINAL INDIGESTION IN CHILDREN  
ON THE BASIS OF THE EXAMINATION OF THE STOOLS  
AND CALORIC VALUES.<sup>1</sup>

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ALTHOUGH a great deal has been written about the importance of the examination of the stools and the caloric estimation of the food in the feeding of infants during the last few years, especially in Germany, and considerable attention has been devoted to these points in the treatment of the digestive disorders of adults all over the world, but little has been done along these lines in relation to the feeding and treatment of the disturbances of digestion in children. There is, in the first place, very little available data as to the caloric needs of children of various ages or as to their metabolism. It is apparently taken for granted that the metabolism of children is essentially the same as that of adults. It is generally believed that young children require a relatively large proportion of carbohydrates in their food and that, as they must not only replace old but also build new tissues, they need proportionately more proteins than adults. None of these points has, however, so far as we know, been scientifically proved.

<sup>1</sup> Read at a meeting of the Pediatric Section of the New York Academy of Medicine, December 9, 1909.

It seemed to us that, if the stools of children suffering from disturbance of digestion, especially of the intestinal type, were examined in order to determine what constituents of the food were not being utilized and the diet regulated on the basis of these findings, due regard being paid to the caloric needs, much better results could be obtained than by the usual empirical methods. Our experience in the treatment of such cases along these lines leads us to believe that these suppositions were well founded. Our experience also leads us to believe that in most instances it is not necessary to make use of complicated methods of examination of the stools, but that comparatively simple tests, such as any practitioner can easily and quickly perform, are sufficient to give results accurate enough to form the basis for satisfactory treatment. We have also found that, with a little practice, it is a very simple matter to calculate the caloric value of the food and to regulate the proportions of fat, carbohydrates, and proteins. Strange as it may seem, we have also found that it is easier to control the diet of the child than that of an adult, and that it is at least as easy to get the coöperation of a child in carrying out the diet as it is to get that of an adult.

**CALORIC NEEDS OF CHILDREN.** Before taking up the treatment of these cases it will perhaps be well to sum up what we know as to the caloric needs of children, to consider the caloric value and composition of the various articles which make up the diet of the average child, and to state briefly the methods employed in the examination of the stools.

There is, as already stated, very little data as to the caloric or protein needs of children. The most valuable observations are those of Camerer,<sup>2</sup> which are based on a prolonged study of his own children. Czerny and Keller have collected and analyzed all the literature on this subject up to 1906 in their work on *The Nutrition of the Child*,<sup>3</sup> while Selter has also summarized it in a recent article on "Functional Disturbances of the Digestive Tract in Childhood."<sup>4</sup> The figures of these observers vary pretty widely as to the caloric needs of children. It is probably not far from the truth, however, to say that the average child of four years needs, in round numbers, about 1200 calories, or 70 calories per kilo, in twenty-four hours; the average child of eight years, 1400 calories, or 60 calories per kilo in twenty-four hours; and the average child of twelve years, 1600 calories, or 50 calories per kilo in twenty-four hours. These facts are perhaps shown better in the following table:

Age.	Total caloric need.	Calories per kilo.
4 years . . . . .	1200	70
8 years . . . . .	1400	60
12 years . . . . .	1600	50

<sup>2</sup> Stoffwechsel des Kindes. Tübingen, 1896.

<sup>3</sup> Die Kindes Ernährung, etc., 1906.

<sup>4</sup> Archiv. f. Kinderheilkunde, 1906, li, 54.

The data as to the protein needs of children differ even more widely than do those as to the total caloric needs. The following table, showing in round numbers the average protein need for twenty-four hours at various ages, is probably approximately correct.

Age.	Total protein need.	Protein need per kilo.
4 years. . . . .	55 grams	3.5 grams
8 years. . . . .	60 grams	3.0 grams
12 years. . . . .	75 grams	2.5 grams

The subtraction of 5 grams from these average figures for the daily protein need in the case of girls and the addition of 5 grams in the case of active boys will make them more nearly correct. It must be remembered that these figures are for the average protein need, and not for the minimum protein need, which is, roughly, about two-thirds the average. In disturbances of protein digestion and in instances in which it is difficult to get children to take food, it is probably safe, therefore, to give only two-thirds of the above amounts, even for considerable periods of time. At any rate, there is no objection to giving much larger amounts of proteins in order to meet the caloric needs when there are disturbances in the digestion of the fats or carbohydrates. On general principles, however, it is wiser to keep the proteins down somewhere near the average need, because the metabolism of the proteins requires more energy and the products of protein metabolism are more difficult of elimination than are those of the fats and carbohydrates. An excess of proteins, therefore, requires an unnecessary expenditure of energy and is consequently not economical. While proteins may be used as substitutes for fats and carbohydrates, they cannot, of course, be used as substitutes for proteins beyond a certain point, that is, the minimum protein need. Within reasonable limits variations in the relative amounts of fats and carbohydrates in the diet probably make no difference to the average well child, the relative amounts taken depending largely on the habits and tastes of the community, of the special family, and of the individual child. In disturbances of digestion fat may be substituted for carbohydrates and carbohydrates for fat with great advantage, provided the total caloric value of the food is kept up. The fats may be entirely replaced by carbohydrates over considerable periods without doing any harm. There is a certain amount of risk in replacing the carbohydrates entirely by fats, however, because of the danger of developing acid intoxication. In the treatment of disturbances of digestion in childhood this procedure is, however, seldom, if ever, necessary.

**CALORIC VALUE OF FOODS.** We have compiled the following table giving the caloric value and composition of the various foods commonly given to children suffering from disturbances of digestion. These figures, while not absolutely accurate are, we believe, accurate enough for practical purposes. It has seemed to us sufficiently

accurate and certainly much more simple and practical to calculate the food values of ordinary helpings of cooked food rather than of weighed portions or of uncooked foods. We have found it very easy to determine from this table not only the caloric value of the child's food but also the amounts of proteins, fats, and carbohydrates. With it we have also found it very easy to plan out a diet for a child to give not only the proper number of calories, but also the desired relations between the different food elements.

TABLE OF FOOD VALUES.

	Calories.	Grams.		
		F.	C.	P.
Whole milk, 1 quart.....	670	38	43	34
Skimmed milk, 1 quart.....	400	10	43	35
Gravity cream, 1 pint.....	860	77	22	14
Buttermilk, 1 quart.....	360	5	43	35
Whey, 1 quart.....	260	5	43	9
Beef juice, 1 ounce.....	10	..	..	2
Crackers, 1 ounce <sup>5</sup> .....	120	3	20	3
Bread, 1 slice <sup>6</sup> .....	75	0.5	15	3
Zwieback, 1 slice <sup>7</sup> .....	120	3	20	3
Shredded wheat biscuit.....	105	0.5	22	3
Oatmeal and other cereals (cooked), 1 tablespoonful.....	25	..	5.5	1
Rice (cooked), 1 tablespoonful.....	45	..	10	1
Potato, size of large egg.....	100	..	20	2
Macaroni (cooked), 1 tablespoonful.....	30	0.5	5	1
Egg { whole.....	72	5	..	7
yolk.....	60	5	..	4
white.....	12	..	..	3
Meat, fish (cooked), 1 ounce <sup>8</sup> .....	60	3	..	7
Butter, 1¼ inches cube = 1 ounce.....	225	24	..	..
Olive oil, 1 tablespoonful.....	125	14	..	..
Sugar (cane), 1 rounded teaspoonful.....	25	..	6	..
Sugar (milk), 1 rounded tablespoonful.....	60	..	15	..
Green peas (cooked), 1 tablespoonful.....	40	..	7	3
Carrots, squash, turnip (cooked), 1 tablespoonful.....	30	..	6	1
Orange (medium sized).....	50	..	13	..
Apple (medium sized).....	70	..	17	..

Clear soups and broths made without rice or barley have practically no nutritive value.

The nutritive value of the "fodder" vegetables—such as spinach, string beans, asparagus, lettuce, tomatoes, and cucumbers—is so slight that it may be disregarded.

**CHARACTERISTICS OF THE CHILD'S STOOL.** Before taking up the methods used in the examination of the stools it may be well to summarize in a very general way some of the characteristics of the child's stool. This is normally homogeneous in consistency. Lumpy and mushy stools are pathological. The former are found when

<sup>5</sup> Crackers vary so much in size that they must be weighed to determine how many it takes to weigh an ounce.

<sup>6</sup> Bread—a slice = 4 inches square and three-eighths inch thick = 1 ounce.

<sup>7</sup> Zwieback—1 slice = large slice.

<sup>8</sup> The lean of a lamb chop weighs about an ounce; so does a piece of meat about 1¼ inches cube.

there is an excess of milk, meat, or eggs in the diet or when the child is underfed; the latter when there is an excess of foods which have a considerable indigestible residue, such as coarse bread, fruit, and vegetables. Large masses of undigested food are usually the result of improper mastication. The reaction to litmus paper is weakly alkaline, weakly amphoteric, or neutral. A very strong alkaline reaction, especially if accompanied by a putrefactive odor, suggests protein putrefaction. A strong acid reaction, associated with a rancid odor, suggests disturbance in the digestion of fat; if associated with the odor of lactic or acetic acid, disturbance in the digestion of carbohydrates. The movement is often frothy or shows bubbles here and there in the latter condition. Microscopic examination shows a few remains of a vegetable nature, single yellow masses, supposed to be albuminous remains, a few muscle fibers, a few crystals, rare starch granules, and microbes which may stain blue with Lugol's solution. The background is granular and made up of the bodies of bacteria and intestinal secretions. When acetic acid is added, a few drops of fatty acid are seen in each field after heating.

**TYPES OF PATHOLOGICAL STOOLS.** Several of the types of pathological stools are characteristic enough to deserve special mention; these are the fatty stools, the stools of carbohydrate indigestion, and the catarrhal stools.

The *fatty stools* are gray or white in color, dry or of clay-like or creamy consistency, acid in reaction, and of a rancid odor. Microscopically they show a large excess of fat in various forms.

The *carbohydrate stools* are brown or golden-yellow in color, salve-like in consistency, acid in reaction, acid or sour in odor. Microscopically they show undigested starch and often an excess of Gram-positive bacteria. If the examination is hasty they may often be mistaken for normal stools.

The *catarrhal stools* show an excess of mucus both macroscopically and microscopically. The stool may be almost entirely composed of mucus or the mucus may be distributed through it. It is often associated with protein putrefaction and a foul odor.

Types less frequently met are those in which there are a large excess of undigested muscle or connective-tissue fibers. Mixed forms are more common than the pure types and more different to interpret.<sup>9</sup>

**METHODS OF EXAMINATION.** The methods employed in the examination of the stools in our cases were as follows: The child's diet, especially in the early years, is almost always a simple one in comparison with that of the adult and in most instances resembles so closely the test diets recommended by Selter and Schmidt that it is possible to draw the same conclusions from the examinations of

<sup>9</sup> A detailed description of the various types of stools can be found in Selter's article in the *Archiv f. Kinderheilkunde*, 1909, li. 54.

the stools as when the test diets are given. Test diets were, therefore, not used in any of our patients. The character and the quantity of the food taken in the preceding twenty-four or forty-eight hours was known in every instance, however, so that for all practical purposes the children had had a test diet.

During the past two years one of us (Talbot) has controlled the results of the microscopic examination of the stools by numerous quantitative chemical examinations and has found that a very accurate estimate of the amount of fat and protein in the stool can be obtained by a simple microscopic examination. In most instances, therefore, no quantitative chemical analyses were made. No attempt was made to verify the microscopic findings as to starch by chemical examination, it being taken for granted, that, if there was no excess of starch under the microscope, it was properly digested. This conclusion is probably correct enough for every-day clinical work, although there is no doubt that starch may be present in the stools when it cannot be detected by the microscope.<sup>10</sup> The methods followed were essentially those described by Schmidt.<sup>11</sup>

*Macroscopic Examination.* The form, coherency, consistency, color, and odor, and the presence or absence of extraneous matters such as pus, blood, mucus, parasites and curds, are noted. If the stool is homogeneous only one part is tested with litmus paper for the reaction. If the stool varies in composition the reaction is tried in several portions. This is done by placing two moistened pieces of litmus paper (red and blue) upon (not in) a fresh surface of the stool.

*Microscopic Examination.* The microscopic portions are examined first with a low power objective and later with a No. 7 objective to bring out the detailed structure. If the feces are hard they are first rubbed up with a little water, otherwise they are thoroughly mixed and three small portions are placed on a slide. The first is crushed out very thin under the cover glass and examined in the fresh condition. Another is stained with Lugol's solution (iodine, 2; potassium iodide, 4; distilled water, 100) and examined under the cover glass for starch. The third is stained with a saturated alcohol solution of Sudan III.

In the first specimen any excess of undigested muscle fibre, connective tissue, or vegetable fibers can be studied, and pathological elements, such as blood, pus, and eggs of parasites, differentiated. A preliminary estimation of the amount of neutral fat, fatty acids, soaps, and starches can also be made. Under the cover glass the starch granules will stain blue or violet and certain microbes will stain blue. There are practically no unchanged starch granules

<sup>10</sup> Rosenheim, *Pflüger's Archiv.*, xlii, 428; Strassburger, *Deuts. Archiv. f. klin. Med.*, lxi, 590.

<sup>11</sup> The Test Diet in Intestinal Diseases.

in a normal stool. An excess is always pathological. (It is important to remember in this connection that almost all baby powders contain starch. Their presence, therefore, must be ruled out.) Iodophilic bacteria, or those which stain blue with Lugol's solution, are suggestive of an early disturbance in the digestion of starch. Under the third cover glass neutral fat drops and fatty acid crystals stain red. Soap crystals do not stain with Sudan III. After this cover glass is examined and the microscopic picture is clear, a drop of glacial acetic acid is allowed to run under the cover glass, is thoroughly mixed in, and then heated until it begins to boil. This process turns the soaps into neutral fat and fatty acids, which, while warm, appear as large, red, stained drops, and upon cooling crystallize. They usually retain the red stain. Any increase in the amount of fat after the addition of acetic acid indicates the presence of a corresponding amount of soaps. An excess of neutral fat indicates that the digestion of fat is not carried on normally, and an excess of fatty acids and soaps that the digestion is normal but assimilation is abnormal.

**ILLUSTRATIVE CASES.** In a not inconsiderable number of instances the difficulty in digestion is due more to an excess in the quantity of food than to errors in the quality. The following case is an example:

**CASE I.**—A boy, aged four and one-half years, was on a very carefully regulated diet. He was, nevertheless, having from five to six large, loose movements, macroscopically digested, daily, and was losing in weight. He had an enormous appetite and his mother had allowed him to eat as much as he wanted, although she had been careful not to give him anything outside of the prescribed diet. It was found that the caloric value of his food was nearly twice as great as was necessary. The quantity as well as the quality of his food was then regulated so that he got only a little more than enough to cover his caloric needs. The number of movements immediately dropped to two a day and he began to increase in weight.

It is very easy, in attempting to regulate the diet to the child's digestive capacity, to err on the other side and give an insufficient amount of food. It is also very easy, if the stools are not examined, to make up one's mind that a patient cannot digest certain food elements, and hence to cut them out of the diet unnecessarily. The following case is an example of both of these mistakes:

**CASE II.**—A girl, aged five and one-half years, that had been treated for chronic intestinal indigestion by another physician for the preceeding six months, came into our hands. During that time she had been taking only modified milk and a little meat. It was said that she could not digest starch. She was having two movements daily, which were said to be foul and to contain mucus. She had not gained in weight for a year. It was found on calculation that the caloric value of her food was somewhat below the normal



and that it contained a large excess of proteins. Measured amounts of bread, cracker, and butter were immediately added to her diet. Examination of the stools a few days later showed that she was digesting the starches as well as the fats and proteins. The amount of starch in the diet was rapidly increased and the modified milk replaced by whole milk, the caloric value of the food being increased to meet her needs. She began to gain in weight at once, gaining four pounds in the first month. Further study showed that she was able to digest all the food elements normally and to eat an ordinary, reasonable diet for her age. The mucus quickly disappeared from her movements on the more liberal diet. The advantages of the calculation of the caloric value of the food and of the examination of the stools in this instance are self-evident.

In many, or perhaps most, instances it is not so much the total caloric value of the food that is at fault as an improper balance of the different food constituents. In such instances there is usually a large excess of some one element. The following cases are examples:

CASE III.—A boy, aged two years, had been losing color and weight for about three months. He was not as vigorous as in the past, but did not seem really sick. He had not vomited, but had had two movements daily, which the mother said seemed normal in every way. She thought that he had not been eating enough, and in order to fatten him had given him a rich Jersey milk with extra cream. The mother, being a Southerner, had also given him corn bread and bacon. Analysis of his diet showed that he was getting 1200 calories per day, while his caloric needs were approximately only 1000 calories per day. His apparent loss of appetite was presumably due to the excessive richness of his food. He was rather thin and flabby and somewhat pale. Otherwise the physical examination showed nothing abnormal. He was given a reasonable diet. The cream, corn bread, and bacon were stopped and the milk changed from Jersey to Holstein. He gained a pound on this diet in the next two weeks, but did not improve as much in his general condition as his mother thought he should. His case was therefore gone into more carefully.

His diet March 1 consisted of milk, 34 ounces; cereal, 4 tablespoonfuls; beef juice, 2 tablespoonfuls; bread, three slices, and a baked potato. This gives a total of about 1150 calories and contains, in round numbers, 40 grams of fat, 130 grams of carbohydrates, and 50 grams of proteins. He had two movements during the twenty-four hours. The second one was small, yellow, semisolid, of foul odor and alkaline reaction, and contained a small amount of mucus. Microscopically it showed considerable undigested starch and many iodophilic bacteria. There was no undigested neutral fat or fatty acid, but a moderate excess of soap and a small amount of mucus.

On the basis of these findings the amount of starchy food was cut down and meat added to his dietary. His diet March 8 was made

up as follows: Milk, 33 ounces; cereal, 2 tablespoonfuls; bread, two slices; a baked potato, and two small slices of chicken. This gives about 1050 calories and contains, in round numbers, about 40 grams of fat, 105 grams of carbohydrates, and 50 grams of proteins. His movement was brown, soft, of uniform consistency, alkaline in reaction, and contained a very small amount of mucus. Microscopically it showed a slight excess of neutral fat and fatty acids, but no excess of soaps or meat fibers. There was no undigested starch. The amount of milk was then cut down and that of the starch slightly increased. From this time on the improvement was steady and uneventful.

CASE IV.—A boy, aged two and one-half years, was brought because of a large abdomen which had been steadily increasing in size for about six months subsequent to a rather severe attack of diarrhoea. Tubercular peritonitis had been suspected. His appetite was always good, often enormous, occasionally capricious. There was no nausea or vomiting and only a moderate amount of flatulence. The bowels moved two or three times daily, the movements being very large, but soft. On passage they were like strips of tape, but on standing formed a homogeneous mass. He had lost considerable weight and on that account was being given rich milk, extra cream, and a great deal of butter. His parents were about to begin cod liver oil also. He was unable to get about much because of the large size of the abdomen. He did not complain of pain and had never been jaundiced.

He was considerably emaciated and moderately pale. His tongue was nearly clean. The liver and spleen were not palpable. The abdomen was very large. The circumference of the chest at the nipples was 49 cm.; that of the abdomen at the costal border, 59.5 cm.; and that at the navel, 56 cm. There was no dulness in the flanks, no fluid wave, no muscular spasm and no tumor.

His movement was very large, unformed, of uniform consistency, soft and spongy, white, with a slightly yellowish tinge. The odor was foul, the reaction alkaline. There was a small amount of mucus intermixed. Under the microscope practically the whole field was made up of soap splinters. There was rarely a neutral fat drop, but no fatty acids or calcium soap. There was very little mucus, no meat fibers or undigested starch. Gram-decolorizing bacteria predominated. There was an occasional large "blue bacillus" and many Gram-staining bipolar bacilli and cocci, but no bifid bacilli.

In this case the chronic duodenal indigestion and the consequent weakening of the power of assimilating fat had been entirely overlooked because of the general emaciation and the enlargement of the abdomen, and the worst possible form of diet prescribed. One familiar with the condition would undoubtedly have been able to

make the diagnosis without the microscopic examination of the stool. It, nevertheless, furnished important corroborative evidence.

Sometimes the microscopic examination of the stools will give warning of impending trouble several days before the appearance of any symptoms or macroscopic changes in the movements. In fact, the movements may appear normal even when there is a considerable excess of fat in the form of soap. The following case is an example:

CASE V.—A girl, aged two years, had been running down for some time, and had grown steadily worse on the diets prescribed by several physicians, all of which had contained a large amount of fat. The examination of the stools had disclosed the cause of the trouble and she was doing very well on a diet almost free from fat. After a time it was thought wise to try to work fat into the diet again. Two ounces of each ten ounces of skimmed milk was, therefore, replaced by whole milk on September 12. The mother reported September 16 that the little girl was doing well in every way. The movement, which macroscopically was perfectly normal, showed under the microscope a considerable excess of fat. The mother found the child out of sorts on her return home, irritable, the appetite poor, and the movements undigested. It was several days after the whole milk was stopped before she was right again and the stools normal.

The finding of vegetable and fruit fibers in excess, both microscopically and macroscopically, is not uncommon and explains a good many cases in which the movements are too frequent and too large in amount. It also explains a certain number of cases of constipation.

It would be very easy to detail many other cases illustrating the same and similar points, but it seems to us that those given are sufficient to demonstrate the advantages of the regulation of the diet in the intestinal indigestion of children on the basis of the findings in the stools and the caloric values of foods over the old "hit or miss" methods.

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## THE TREATMENT OF HEMORRHAGE FROM GASTRIC ULCER.

WITH SPECIAL REFERENCE TO GASTRIC LAVAGE.

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WHENEVER severe hemorrhage occurs in gastric ulcer it not only frightens the patient, but often enough the physician as well. The physician, however, should not forget that fatal bleeding from gastric ulcer is comparatively rare, as is seen from the statistics of

men who personally have followed a large series of ulcer cases. Fenwick<sup>1</sup> states that death due to uncontrollable hemorrhage has occurred in 3.4 per cent. of his cases; von Leube<sup>2</sup> gives his proportion as 1 per cent.; Jacoby<sup>3</sup> also gives 1 per cent.; while Ewald<sup>4</sup> claims that with his large experience he has never seen a fatal issue caused directly by profuse hemorrhage. A number of other authors<sup>5</sup> figure between 3 and 5 per cent., so that we may put the average at about or below 3 per cent.

We do well to keep these facts in mind, particularly when confronted with hemorrhage of a severe type. With moderate hemorrhages the immediate danger to life is not great, although they may become dangerous when often repeated, thereby gradually undermining the vitality of the patient. The frequent occurrence of small or moderate hemorrhages may call for surgical treatment in order to prevent further bleedings and to arrest the development of cachexia which often follows the frequent loss of blood. I must abstain, however, from discussing this specific indication, since it is the principal object of this paper to deal with the *direct* treatment of active bleeding. I only wanted to point out that repeated hemorrhage of moderate severity, although for the time being not dangerous to life, may prove much more dangerous for the final outcome than those alarming excessive hemorrhages.

With spontaneous and very profuse bleeding, the severe anemia resulting from the sudden great loss of blood brings about changes in the system, which if undisturbed, of themselves tend to arrest the bleeding. The vasoconstriction which goes with the advent of sudden anemia and with syncope allows the bleeding vessel to contract, and the low activity of the heart, permit the formation of a thrombus.<sup>6</sup> The formation of a thrombus is particularly necessary in those cases of chronic ulcer "where the eroded artery lies like a rigid pipe in the fibrous wall of the ulcer, and being unable to contract, can only become occluded by the process of clotting" (Fenwick, p. 135). When the clotting is not quickly and efficiently accomplished, such patients may bleed to death very rapidly. A postmortem examination may show that the ulcer after penetrating through the whole gastric wall had eroded a larger branch of the arteria pancreatica or lienalis, or one of the main arteries itself. The finding of the anatomical conditions demonstrates that probably no medical treatment could have checked the bleeding and on

<sup>1</sup> Ulcer of the Stomach, p. 199.

<sup>2</sup> Verhandlung. der Gesellsch. f. Chirurgie, 1897.

<sup>3</sup> Congr. Amer. Phys. and Surg., Med. Record, 1897.

<sup>4</sup> Deutsche Klinik, v, 508.

<sup>5</sup> For further statistics: see Lieblein, Deutsche Chirurgie, xlv, 100, and Bamberger, Die Behandlung des chron. Magengeschwürs Verl. Julius Springer, 1909, 24.

<sup>6</sup> Von den Velden (Arch. f. exp. Path. u. Pharm., 1909, lxi, 37), lately demonstrated that after each hemorrhage the influx of serum from the tissues into the blood carries with it a great deal of thrombokinase, a substance which is present in all tissues and greatly increases the coagulability of the blood.

the other hand leaves it often very doubtful whether surgery could have accomplished it.

Owing to the rapid course in most of these cases we usually find the patient so exsanguinated that the result of an operation becomes very problematical, especially when we consider the great difficulties that are often met with even postmortem in trying to locate the bleeding. We must remember that excessive bleeding not only originates from eroded arteries at the base of the ulcer, but also from ruptured veins around the ulcer, or from minute erosions at distant points, so that even resection of the ulcer may fail to remove the source of the bleeding. Without denying the possibility of checking the bleeding by surgical means, the conditions present are as a rule unfavorable for a successful operation. We must therefore console ourselves to the fact that a certain number of cases are lost, no matter what treatment we may try. Luckily these cases are not frequent, as we learned from the small total percentage of fatal hemorrhages already stated.

In dealing with excessive hemorrhage we should not be influenced too much by such experiences. We do far better to base our plan of treatment on the knowledge of what actually happens when the bleeding comes to a standstill. As we have argued before, it is either vasoconstriction or the forming of a thrombus which brings about hemostasis, both processes developing with the effect of anemia and of the weakened action of the heart. Nothing seems therefore more out of place than the routine treatment usually met with, which directs all efforts toward overcoming the depressed condition of the circulation. Yet from a large experience I can state, that the attempt to strengthen the weakened heart by administering heart tonics, infusions of salt solutions, etc, is greatly overdone by most physicians; as a rule it dominates the whole plan of treatment and not infrequently is the only treatment instigated. When the desired effect of energetic stimulation has been reached, the vigorous action of the heart will eventually result in freeing a freshly formed thrombus and thus cause a renewal of the bleeding. Since the continuation of the bleeding forms the main danger of such situations, it is obvious that energetic stimulation may increase the danger by bringing about exactly what we should try to prevent. For this reason it must be considered unwise to resort indiscriminately to vigorous stimulation.

We are all the more justified in abstaining from energetic stimulation, as general experience teaches that most cases with profuse hemorrhage, when not ending fatally on account of uncontrollable bleeding, overcome anemia and disturbance of circulation surprisingly well. It may sound paradoxical, yet it is a fact that just such cases of chronic ulcer, which at one time or other had a very profuse hemorrhage, give the best end results both in regard to the palliative and the curative treatment of the ulcer.

As an illustration I briefly give the history of a woman who after suffering for several years from chronic ulcer, at the age of thirty-six, went through an extremely severe gastric hemorrhage. She was so exsanguinated and presented such marked evidence of progressive heart failure, that Dr. F. Lange, who saw the patient with me, declared her moribund. Nevertheless during the spell of great weakness the bleeding stopped and the patient gradually recovered from this apparently hopeless condition. After a long continued dietetic treatment, while increasing both in weight and strength, she lost all symptoms of gastric ulcer and has since then (over ten years now), remained perfectly well. I could mention a number of similar instances which show that anemia and weakness of the heart may prove helpful in bringing about cessation of the hemorrhage and in the majority of cases are well tolerated, provided the bleeding stops.

A former generation of physicians who were familiar with the effects of venesection realized the importance of such observations. When confronted with uncontrollable hemorrhage, they would perform a venesection, expecting to have the bleeding stopped by the resulting syncope and its effect upon the circulation. When the venesection is performed according to the rules given by Marshall Hall, with the patient sitting upright and a quick flow of the blood is secured, it leads more easily to syncope and thereby eventually to the control of the internal hemorrhage. I saw Kussmaul successfully carry out this principle in a case of extreme hemoptysis, in which the patient within a short time lost enormous quantities of blood. All accessible methods of hemostasis were tried in quick succession without result, when finally a full venesection caused syncope and with it brought the bleeding to a standstill. We find the same principle in another method, which, less heroic than venesection, tries to imitate its effect by applying elastic ligatures to the four extremities. As a result a great quantity of blood accumulates in the limbs and the internal organs become anemic. This method was also successfully employed in cases of severe gastric hemorrhage. I have discussed this question somewhat fully because I have often been impressed by the great activity of physicians in making stimulation the most important part in the treatment of excessive hemorrhage. We should be very reluctant with stimulation, employing it only in case of stern necessity and even then cautiously and judiciously. The paramount issue of the situation is the stoppage of the bleeding and this, as we have seen, is better safeguarded by avoiding stimulation.

As soon as the bleeding has come to a standstill, our efforts should be directed principally toward preventing a recurrence of the bleeding. This is best accomplished by securing complete mental and bodily rest. The patient should be kept upon his back with an icebag on the epigastrium to control the movements of the stomach. A full

dose of morphine helps here more than anything else and at the same time makes it easier for the patient to stand the fasting of the following days. It is essential to give the stomach absolute rest by abstaining from all nourishment. I find it better even to omit rectal feeding during the first few days, because nourishing enemata often provoke peristalsis of the stomach and are known to stimulate gastric secretion (Umber).<sup>7</sup> We must be aware that with any functional activity of the stomach a thrombus might easily be dislodged or dissolved. The danger arising from such an accident is certainly greater than the danger of starvation, providing the fasting is not injudiciously continued for too long a period. During the last few years the Lenhartz treatment has induced physicians to discontinue the traditional starvation period and to feed their patients immediately after the hemorrhage.

The lively discussion which followed Lenhartz's recommendation has certainly demonstrated the fallacy of continuing the starvation period not only for days but for weeks, as has been done. On the other hand it made clear that the views upon which Lenhartz bases his advice are erroneous in some respects. We are here only concerned about the effect of early feeding on a bleeding ulcer. Reports are becoming more numerous that early feeding, according to Lenhartz, caused recurrence of the hemorrhage, thus violating the most important indication, that of preventing a continuation of the bleeding. It is possible that further observations will teach us to single out certain conditions, in which early feeding may be permissible. For a general rule, however, it is safer to adhere to the old principle of having the patient fast a few days after the hemorrhage. How many days and, further, how carefully to feed afterward, should be decided in each individual case.

When the hemorrhage does not stop, the question arises, "What can we do to check the bleeding?" Of the many remedies employed for this purpose, I can only discuss shortly some of the more important ones. Formerly styptics were used a great deal—acetate of lead, perchloride of iron, oil of turpentine, etc. As hemostatics they are very unreliable, while on the other hand they are apt to increase the ever present and annoying nausea and often excite vomiting. The same can be said for the internal use of more modern preparations like ergot. Neither have I ever seen any benefit from ergot preparations given hypodermatically. Calcium chloride in full doses may prove of value in cases in which the bleeding is continuous but slight in amount, but it is slow in its action and will hardly exert any influence in profuse bleeding. Adrenalin has the great disadvantage that the vasoconstriction produced by this drug is followed by a period of vasodilatation, which may eventually cause a renewal of the hemorrhage. As for the results derived from gelatin pre-

<sup>7</sup> Berl. Klin. Woch., 1905, No. 3.

parations given per os or per clyisma, the reports are as yet very doubtful, and when given subcutaneously it may cause tetanus, unless the preparation is absolutely reliable. As several days are required to obtain a freshly sterilized preparation, it is likely to arrive too late,

Very promising seems the employment of serum, which has recently been introduced for the treatment of hemophilia. So far I only once had occasion to observe the administration of diphtheria serum in a case of fatal gastric bleeding, from a ruptured varicose vein. The case was so peculiar that it allows no opinion as to the effect of the serum. The same patient also received escalin (aluminum-glycerin paste), which is highly praised by Klemperer;<sup>8</sup> others counsel against its use on account of the bad results which they observed.

The most reliable of the internal remedies is bismuth, which is largely used in the treatment of gastric ulcer since Kussmaul and Fleiner's recommendation. The crystalline bismuth subnitrate is preferable because, as Matthes<sup>9</sup> has shown, this salt sticks to the surface of the ulcer, accumulates there and thus makes a protective coating for the ulcer.

Naunyn<sup>10</sup> reports a case, in which lavage of the stomach followed by the administration of bismuth stopped a profuse gastric hemorrhage. The patient who at the same time suffered from excessive diarrhoea, died from exhaustion and severe anemia. She had received 20 grams of bismuth subnitrate thirty-six hours before death and twenty-four hours later an additional 5 grams. Autopsy showed that the ulcer was filled by a clump of bismuth about 20 grams in weight, while the remainder of the stomach contained but a very small quantity. Naunyn's experience demonstrates that we may expect a more efficient action of bismuth when the stomach is previously emptied by lavage.

This leads me to the discussion of the method, which I consider of greatest importance in the control of gastric hemorrhage, namely gastric lavage. Since I first saw lavage performed in cases of bleeding ulcer at Kussmaul's clinic more than twenty-five years ago, I have employed this treatment in a series of cases of profuse hemorrhage, in almost every case with favorable result. I have no hesitation therefore in recommending gastric lavage as the most expedient means in the treatment of severe hemorrhage, provided it is carefully applied.

As I am well acquainted with the aversion which most physicians harbor against this procedure, I shall discuss the pros and cons in detail. The most frequent objection raised against lavage is that it may cause perforation. Perforation, however, only takes place

<sup>8</sup> Therapie der Gegenwart, 1907; Jacobson, Therapie der Gegenwart, 1909.

<sup>9</sup> Centralbl. f. innere Med., 1894.

<sup>10</sup> Deutsch. med. Woch., 1898; Vereinsbeilage, No. 3.



after the ulcer has penetrated the different layers of the stomach and has led to necrosis of the serosa. This is evident when we examine the anatomical features of the opening. As a rule the opening is small and circular, showing the defect produced by necrosis. I have found this condition in a case that I reported,<sup>11</sup> in which perforation set in one hour after the stomach was washed in order to prepare the patient for the previously planned gastroenterostomy. The same condition was found in similar cases. To my knowledge nobody has ever reported that the perforation opening was a lacerated tear through non-necrotic tissue, a finding which would prove that the perforation was a direct result of lavage. This, too, could only occur by forcibly overdistingending the stomach by great quantities of water, a possibility which we may well ignore, if ordinary precautions are observed. With a carefully performed lavage the danger of causing perforation by overdistention, is out of the question. On the contrary, lavage exerts its greatest benefit by doing away with the real cause of overdistention, by removing the large quantities of accumulated blood, acid secretions, food remnants, and gas, which are usually present in such cases, often producing an enormous distention of the stomach. We can therefore dismiss the objection that gastric lavage may cause perforation. If it should happen incidentally, that lavage is undertaken just before the threatening perforation actually occurs, the cleaning of the stomach will prove very beneficial in preventing the escape of stomach contents through the perforation, thereby greatly improving the prognosis. In my case cited before, the good result obtained by resecting the perforated ulcer must to a great extent be credited to this fact. It is well known that the prognosis is far better when perforation takes place at a time when the stomach is empty.

A further objection to lavage is that it disturbs the complete rest of the stomach, which as we have seen before, is essential in order firmly to secure the freshly formed thrombus. This is perfectly correct, when the hemorrhage has ceased and we may assume that an efficient thrombus has been established. However, conditions are altogether different when the bleeding continues, because then either no thrombus has developed, or if formed, does not completely fill the opening of the vessel. We know from general surgical experience that such a partially occluding thrombus is often the cause of continued bleeding. The removal of such inefficient thrombi is not only not dangerous, but on the contrary it is a necessity in order to give the bleeding vessel a chance to contract or to form a more efficient thrombus. From what I have seen this explanation holds also true for gastric hemorrhage, because I observed in several instances, that the bleeding ceased suddenly during the act of lavage. This shows how unjustified is the traditional rule handed down in

<sup>11</sup> Kaufmann, AMER. JOUR. MED. SCI., April, 1904.

all text-books, that lavage is absolutely forbidden in gastric hemorrhage. It should certainly not be condemned in such general fashion, because lavage may prove the best procedure to stop the bleeding.

Finally comes the objection that the introduction of the tube is difficult and exciting for the patient. When lavage is given by a physician experienced in this method he will overcome the difficulties in inserting the tube, particularly when he wins the patient's confidence by his assurance. As a rule I was able to insert the tube, even with the patient lying on his back without causing excitement or great exertion. It is advisable to insert the tube just far enough to secure siphonage and to limit the quantity of water used each time to about 300 c.c.

As for the advantages of lavage, I have already mentioned the release of partially occluding thrombi. A further very striking advantage is the benefit of lavage when the stomach is distended by large quantities of contents. These stagnating masses are usually very sour and fermenting, and their presence not only causes nausea and pain, but acts very harmfully by constantly irritating the mucous membrane to intense hypersecretion, thereby further increasing the amount of gastric contents. Again, the fermentation always connected with such conditions invariably leads to pronounced and sometimes to enormous gas distention of the stomach, so that when the tube is introduced the contents shoot out under high pressure, even, as I have experienced, with an explosive sound. It seems hardly necessary to explain how detrimental such a distention is in every respect. No doubt it is frequently the direct cause of the continuation of the bleeding. The removal of the fermenting masses not only relieves annoying symptoms of gastric irritation, but eventually brings about a direct cessation of the bleeding by allowing the emptied stomach to contract and this aids in the occlusion of the eroded vessel.

The evacuation of the stomach and the contraction which follows it are of the greatest importance for the improvement of circulatory disturbances. I saw cases of gastric hemorrhage in which the pronounced symptoms of insufficiency of the heart were only in part due to anemia, but to a much greater extent they were caused by the pressure of the gas distended stomach against the diaphragm and heart. In these cases circulation was at once improved when the stomach was emptied, while the anemia remained unchanged. I had a very instructive case of this type twelve years ago: The patient was a woman, aged thirty years. After excessive gastric bleeding the pulse rose to 160, became fluttering, and the heart action was so weak and irregular, that several physicians connected with the case considered her at the point of death. The stomach was full and so distended that it almost reached the level of the axilla. After the stomach was emptied, the pulse rate immediately came down to 116, the heart action became stronger, and the patient recovered.

The understanding of such conditions has been greatly advanced by the recent study of acute gastric dilatation. The knowledge of this clinical picture is not quite as new as some writers would make us believe. At any rate acute gastric dilatation is frequently associated with gastric hemorrhage. It is generally admitted that the most rational and the most effective treatment of acute gastric dilatation is prompt evacuation by lavage. This holds true for cases of acute dilatation in connection with hemorrhage. Let us hope that this discussion will encourage physicians to resort more frequently to lavage in gastric hemorrhage than heretofore.

Of the cases of severe gastric hemorrhage which I successfully treated by lavage, I wish to report as an illustration one which is particularly interesting. The patient, aged thirty-nine years, had suffered for sixteen years from the cardialgic form of chronic ulcer without hemorrhages. In June, 1906, an abscess in the pyloric region was opened; the gall-bladder was found normal and it is probable that the abscess had formed after a perforation of the ulcer. Soon after the operation severe gastric symptoms recurred with evidence of pyloric stenosis. Since these symptoms persisted in spite of prolonged medical treatment we advised operation. In June, 1907, Dr. Willy Meyer performed a posterior retrocolic gastroenterostomy by means of sutures; at the pylorus a hard mass was found producing partial obstruction. Eight hours after the operation hematemesis set in, which in the following twenty-four hours recurred five times, causing such a very great loss of blood that the condition of the patient became very alarming. We decided to evacuate and wash the stomach. At first we obtained large quantities of dark bloody material; then the washings became bright red showing that the bleeding was still active, when suddenly the water returned clear. Before withdrawing the tube a large dose of bismuth subnitrate was poured into the stomach. The bleeding ceased and an uninterrupted convalescence was followed by a perfect cure.

In this case gastric lavage stopped an attack of severe bleeding, which followed a gastroenterostomy, an interesting fact, when we consider that surgeons advise this operation to check excessive hemorrhage. Nor is this experience anything unusual. A number of surgeons in this country and abroad have reported the occurrence of severe hemorrhage following a gastroenterostomy. I mention Mayer,<sup>12</sup> Busch<sup>13</sup> (reporting from Körte's clinic), Clairmont<sup>14</sup> (from von Eiselsberg's clinic), and others. Kocher,<sup>15</sup> in discussing his own similar experiences, confirms Clairmont's view, that the possibility of causing a hemorrhage forms one of the main dangers

<sup>12</sup> Bruns' Beiträge z. klin. Chirurgie, 1908, vi.

<sup>13</sup> Langenbeck's Archiv, xc, 1.

<sup>14</sup> Mittheil. aus d. Grenzgeb. d. Med. u. Chirurg., 1909, xx.

<sup>15</sup> Ibid.

of gastroenterostomy, because in certain cases this operation not only fails to stop bleeding, but on the contrary it may be the direct cause of its occurrence. Kocher therefore advises more radical operations like excision of the ulcer, etc., whenever possible.

It is not my intention to enter here into a discussion of the difficult and as yet unsettled question of surgical treatment for gastric ulcer. I only wish to emphasize that in contemplating operative measures we should distinguish more clearly between operations performed for the purpose of perfecting a final and complete cure of the ulcer and those operations which are undertaken for the immediate control of hemorrhages. I have already discussed the advisability of radical operations in cases in which the ulcer, not yielding to medical treatment, causes frequent hemorrhages, and thereby greatly undermines the vitality of the patient. In such cases, however, it is decidedly better not to operate at the time of acute bleeding. Here the purpose of the operation is not to check a given hemorrhage, but to prevent the occurrence of bleedings. The radical operation necessary to accomplish this, certainly promises better results when performed after the patient has recovered from a hemorrhage. On the other hand, when an operation is undertaken for the very purpose of checking the hemorrhage, it has to be done while the bleeding is active. This surgical indication naturally arises only with very profuse hemorrhages. Unfortunately just in these cases in which we should expect most success from an operation, the conditions as a rule are such, that the operation forms a greater danger than the hemorrhage itself. In the first part of this paper I pointed out the fact, that with the rapidly developed exhaustion of these patients a prolonged operation must become a hazardous experiment. If we want to be reasonably certain of accomplishing anything at all, we must undertake radical, that is, prolonged operations. The quickly performed gastro-enterostomy does not answer; it is, as we have seen before, entirely unreliable. As Deaver states, gastro-enterostomy in acutely bleeding ulcers is worse than useless. Prolonged operations, however, are decidedly more dangerous, the percentage of mortality after radical operations being considerably higher than after gastro-enterostomy, particularly when the operation is undertaken under the unfavorable conditions resulting from excessive hemorrhage. When we further consider that even a radical operation does not always succeed in checking the bleeding, we cannot conceive that this uncertain and risky procedure lessens the danger of the situation. On the contrary, in profuse hemorrhage, the patient stands a better chance of recovery, if treated in the conservative manner described in this paper. It is not probable that radical operations undertaken at the time of the bleeding, will reduce the 3 per cent. mortality usually observed in excessive gastric hemorrhage. We should try, however, to reduce the mortality by improving the methods of medical treatment. In this connection I wish to plead

once more for the more frequent employment of gastric lavage as a direct means of checking the bleeding. It is certainly not superfluous to emphasize the advisability of gastric lavage, when we realize that nowadays physicians can be convinced more easily in favor of laparotomy than for the use of the stomach tube. At all events lavage should be tried before an operation is decided upon. While it can do no harm, lavage will frequently check the bleeding and postpone an operation, which may prove necessary for other reasons. I have no doubt that the good results derived from lavage will do away with the deeply rooted prejudice against using the tube in bleeding ulcer.

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## NORMAL HUMAN BLOOD SERUM AS A CURATIVE AGENT IN HEMOPHILIA NEONATORUM.<sup>1</sup>

A PRELIMINARY REPORT, WITH SUGGESTIONS FOR ITS USE IN  
OTHER CONDITIONS.

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IN a study of a series of cases in which animal serum was administered to human beings it has been noted that certain symptoms appear regularly and in sequence. The first of these and the most frequent is fever, which is usually high and may vary from one to three degrees Centigrade. The fever is irregular and fluctuates in accordance with the amount of serum used, and remains until all other symptoms disappear. Shortly after the beginning of the fever certain rashes appear on the skin, the most troublesome of which is urticaria, which may begin at the site of injection and spread over the trunk and limbs. There may be considerable œdema in the neighborhood of the wheals, and often the itching is very intense and agonizing. Erythema usually follows the urticarial rash within two or three weeks. Scarlatiniform rashes also occasionally appear. Sometimes a morbiliform rash appears, and when it affects the face, accompanied by swelling and lacrymation, with congestion of the conjunctiva, is very suggestive of measles. The lymph nodes on the side of the body to which the serum has been administered first become enlarged and later others over the body. The enlargement is accompanied by tenderness. In some instances the joints become very painful and slightly reddened, and occasionally slight swelling occurs. General œdema of the body may occur and the weight

<sup>1</sup> Read at a meeting of the New York Academy of Medicine, March 31, 1910.

increase, though there is diminished ingestion of food. The œdema may be accompanied by albuminuria and casts and blood in the urine. Some rare manifestations reported are: Hemorrhage into the bowel, urethral hemorrhage, œdema of the glottis, and diffuse bronchitis.

We not infrequently hear of sudden death following soon after the administration of a single dose of antitoxin. Rosenau and Anderson, in 1906, collected 19 cases from the literature and made the statement that they knew of several more that had not been reported. We all know of instances of sudden death following antitoxin injections which have not been reported in medical literature, but if all of these, reported and unreported, were taken together, they probably would not detract from the splendid record of antitoxin more than the minutest fraction of a per cent. These results by no means suggest to us the abandonment of antitoxin, but rather that we should seek some method of separating more completely the antitoxin from the serum, which is the real source of danger.

Von Pirquet and Schick were the first to consider the aforementioned symptoms, which they found in 20 per cent. of the cases receiving antitoxin, and which they studied together as a distinct disease with its definite incubation period of eight to twelve days; they called it the *serum sickness*.

The frequency of the serum sickness depends on the amount of serum used (Park and Bolduan). When 10 to 30 c.c. of serum was used, 22 per cent. of the cases developed serum sickness. Since using concentrated antitoxin with injections of 5 to 15 c.c. of serum, the number of cases developing symptoms has been reduced to 6.5 per cent. Large injections (100 to 200 c.c.) of Moser's scarlet-fever serum produce serum sickness in 85 per cent. of the cases.

Von Pirquet and Schick first demonstrated that a second injection of serum produced more rapid and acute symptoms than a single injection. The first dose has a sensitizing effect; the condition produced is the opposite of prophylaxis and is identical with the hypersensibility produced by Richet in his experiments with congestion and called by him anaphylaxis.

Rosenau and Anderson, in their experimental work on anaphylaxis, have found that in some cases one-millionth of a cubic centimeter intraperitoneally will sensitize a guinea-pig, and that a subsequent dose ten days later of 0.1 c.c. of the same serum will kill the pig. These were exceptionally small doses, but they found the same result quite regularly when larger amounts of a serum were used. Their earlier experiments were made with diphtheria antitoxin, but later, by using normal horse serum, they demonstrated that "the toxic action . . . is caused by a principle in normal horse serum and is entirely independent of the antitoxic properties of the serum."

After establishing that the poisonous principle is inherent in this particular normal serum, they extended their investigations to determine whether it also resided in the normal sera of other animals. For this purpose guinea-pigs were used, and were injected intraperitoneally with the serum of dogs, hogs, cattle, sheep, cats, and rats. Second injections with the same serum have produced either severe symptoms or caused death, producing in these cases anaphylaxis just as does the horse serum. It has been shown that large doses of normal horse serum, as well as small ones, will produce anaphylaxis in the guinea-pigs. By this work the principle that the serum of one species of animal is poisonous and often fatal to a different species has been well established. A point of interest and much importance lies in the determination of the effect of repeated doses of alien serum on the nutrition of animals to which such serum is not fatal. Repeated injections of horse serum practised by Salter in young guinea-pigs caused retarded growth. Dr. Park's experience with repeated injections into young guinea-pigs of normal horse serum, after killing the complement by heating, is that they "tend to become cachectic and die."

Since Harvey's discovery of the circulation of the blood the medical profession at times has had great hopes of finding in the transfer of blood from some healthy source to individuals suffering disease a means of curing many otherwise refractory or incurable maladies. About the middle of the seventeenth century lamb's blood was transfused into the human subject, but it was soon learned that the operation was unsafe, inasmuch as death frequently followed, in consequence of which the practice was discontinued. Many years later direct transfusion was attempted from one individual into the vein of another by means of a cannula. Because of coagulation, thrombosis, etc., the method was abandoned. Attempts have also been made to use intravenously defibrinated blood, but the method is so beset with dangers it is no longer considered safe.

Crile has given us our most recent method of transfusion, and from a surgical standpoint it must be considered an ideal one. A record of the lives that have been saved by this procedure is glowing tribute enough to its merits without entering into any words of praise. However, even here we meet with recitals of sad experiences. It is well known to those familiar with its uses that sudden death sometimes follows the transfer of blood in this way. In these cases air embolism can be excluded as a factor, and we are left with theories to account for the fatalities. Of these, we have red cell embolism, hemolysis, and thrombosis. J. G. Hopkins has demonstrated intravascular phagocytosis of red blood cells. The spreads, made from the blood and bone marrow of a patient who had been transfused and died from the effects, showed polynuclear leukocytes, which had engulfed within their protoplasm from one to five or six red blood cells. This phenomenon suggests the speculation whether,

in the transfer of whole blood from one individual to another, the cellular elements are not just so much foreign material which the recipient must destroy and dispose of, and also whether the main virtue in transfusion does not lie in the serum alone.

Under the name of hemophilia neonatorum I report herewith a series of cases, which includes a number of bleeding babies, the etiology of the hemorrhages in which, as is usually the case, is unknown. In none of the cases was the hemorrhage due to traumatism. Bleeding appears as a rule, during the first week of life, and in this series most frequently on the second, third, and fourth days. The primary

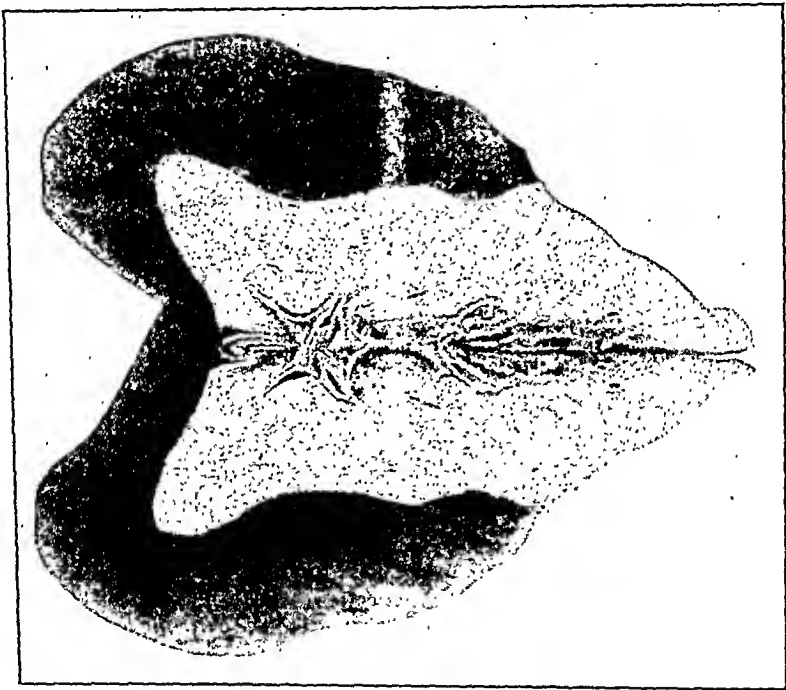


FIG. 1.—Subcapsular hemorrhage of the liver in hemophilia neonatorum.

bleeding may be from anywhere in the skin or mucous membrane surfaces. However, I have found postmortem that the principal hemorrhage may be either in the brain with extensive laceration, or in the liver (Fig. 1), in which case the capsule may be almost entirely dissected from the surface of the organ; and in addition to these, hemorrhagic spots in other internal organs and effusions of blood in the various serous cavities may be found. In some instances I have found the spinal canal filled with fluid blood. The first bleeding may be a slight oozing from the cord at its point of junction with the skin surface and not from the end of the cord due to faulty tying. This cord hemorrhage may persist in spite of all local remedies, and in the course of two or three days a considerable quantity of blood may be lost by this appa-



rently insignificant bleeding. Other bleeding may come from the gastro-intestinal tract, evidence of which is seen in the vomiting of blood or bleeding from the rectum. The lips and gums also frequently bleed. Often the severest hemorrhage appears in the skin, and as a result large hematomas may form which have no relation whatever to traumatism.

Among the list of drugs advocated as therapeutic remedies for this condition the most favorite are probably calcium salts, solutions of gelatin, and adrenalin. Numerous drugs have been employed, but the very length of the list attests their uselessness. In eighteen recorded cases of hemophilia at the Lying-in Hospital, New York, in which these remedies were used there were seventeen deaths, which demonstrates the high mortality in this disease and the futility of all previous therapeutic measures.

Having in mind the almost uniform failure of drugs in this condition and the possibility of producing serum sickness by using the serum of a different species, I decided to attempt the use of normal human serum. In January, 1909, I made my first injections of normal human serum into a bleeding baby.

CASE I.—The subject was three or four days old when it began bleeding. Within twenty-four hours the body was black and blue from subcutaneous hemorrhages; there was a large hematoma occupying one-third of the scalp on one side of the head, and bleeding from the mouth and bowel. The child was so weak it could not cry out when disturbed, though it would make a feeble effort. The case was thought hopeless by the attending surgeon, who requested his house surgeon to ask permission of the parents for a postmortem examination. It was at this time I made the first injection of normal human blood serum; 10 c.c. was used and administered subcutaneously three times during the first day and once each on the following two days. Within a few hours a decided improvement was noted in the condition of the baby, in that the hemorrhages ceased, the old ones began to fade, and strength returned to the child in a very noticeable way. Within three days the hematoma of the scalp was entirely absorbed, and it was quite evident that the child was out of danger. This proved to be true, as the child left the hospital in due time with its mother without any sign of having been a bleeding baby.

Encouraged by this result, the attending physicians of the New York Lying-in Hospital have placed at my disposal for treatment with normal human serum all the bleeding babies that have appeared in their wards. Altogether I have used it in twelve cases, all of which have been cured of their bleeding sickness.

I report herewith eight additional cases, showing the variations in the temperature and weight charts.

CASE II.—First child; female; full term; normal delivery. On the fifth day blood was found oozing from the vulva. During the sixth

and seventh days bleeding was continuous. Two hours after applying a fresh napkin the labia and buttocks would be smeared with blood. On the ninth day there was slight oozing from the umbilicus. There was no bleeding after the ninth day. Normal human serum was administered subcutaneously as follows: On the seventh day, three days after bleeding began, 10 c.c. in two doses; on the eighth day, 19 c.c. in two doses; on the ninth day, 22 c.c. in three doses; on the tenth day, 9 c.c. in one dose; total, 60 c.c. in four days (Fig. 2). The total loss of weight was 450 grams, which was reached on the sixth and remained through the seventh day. When the serum

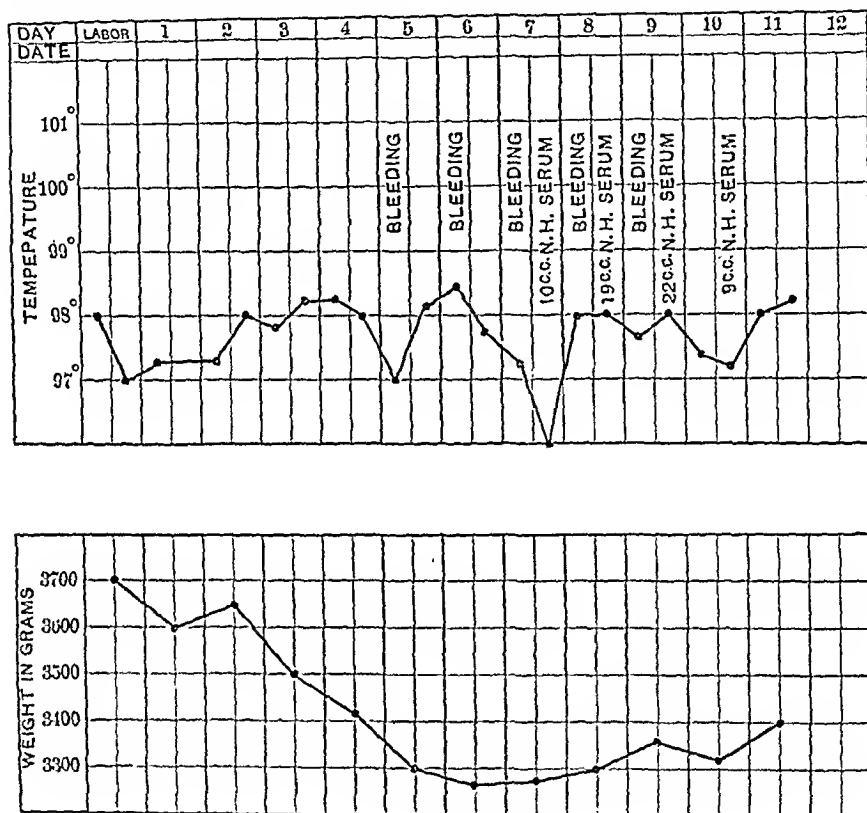


FIG. 2.—Temperature and weight charts of Case II.

was administered the weight began immediately to increase and a steady gain was made later. This baby showed a tendency to sub-normal temperature, which returned to the normal after the bleeding had stopped. It left the hospital in due time in a normal condition.

**CASE III.**—Third child; male; full term; high forceps delivery. It showed no bleeding until the seventh day. Then a dorsal division of the prepuce was made for phimosis. During the next four days bleeding recurred about every four hours, often profuse and difficult to control. There was profuse bleeding from the stump of the cord on the seventh day, which continued on the eighth and ninth days, when the stump was invaginated. On the eighth and ninth days

there was bleeding from the lips and gums, and on the tenth day subcutaneous hemorrhages appeared on the face. Normal human blood serum was injected subcutaneously as follows: On the eighth day, one day after bleeding began, 10 c.c. in one dose; on the ninth day, 40 c.c. in four doses; on the tenth day, 12 c.c. in two doses; on the eleventh day, 14 c.c. in two doses; total, 76 c.c. in four days (Fig. 3). The weight of this child ran down steadily until the tenth day, losing altogether 750 grams ( $1\frac{1}{2}$  pounds). Two days after receiving the serum it gained 100 grams, then lost 50, after which it held its

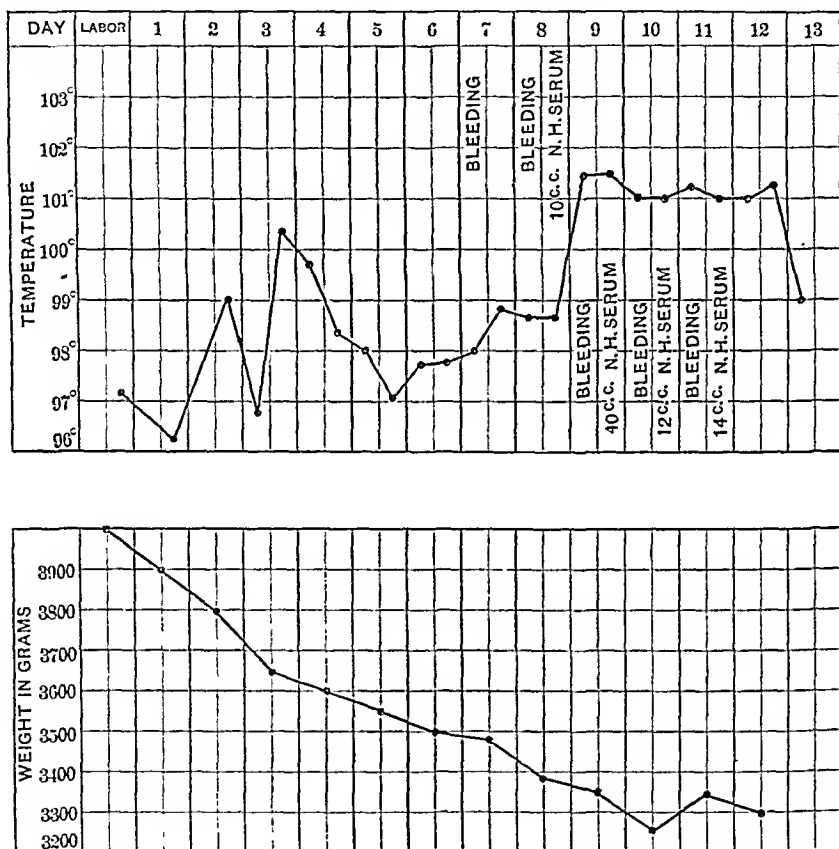


FIG. 3.—Temperature and weight charts of Case III.

own and finally gained. Directly after the bleeding began the temperature rose to  $101.4^{\circ}$ , and it did not go below  $101^{\circ}$  until the bleeding was controlled. This baby was extremely weak and was considered in a serious condition, but was finally discharged from the hospital, with the mother, in good condition.

CASE IV.—Third child; male; full term delivery by Cesarean section. On the second day there was slight bleeding from the nose and mouth, and small hemorrhagic spots appeared on the arms and back. The child had embarrassed respiration, attacks of cyanosis

and nystagmus. On the third day the hemorrhagic spots increased in size. On the fourth day profuse bleeding from the gums and from the bowels occurred. On the fifth day there was more bleeding from the mouth and rectum and more subcutaneous hemorrhages. On the sixth day profuse bleeding from the bowels. On the seventh day more subcutaneous hemorrhages in three places on the body. The baby was too weak to nurse, and was fed from a medicine dropper. At this time subcutaneous injections of normal human blood serum were begun and given as follows: On the seventh day, five days after

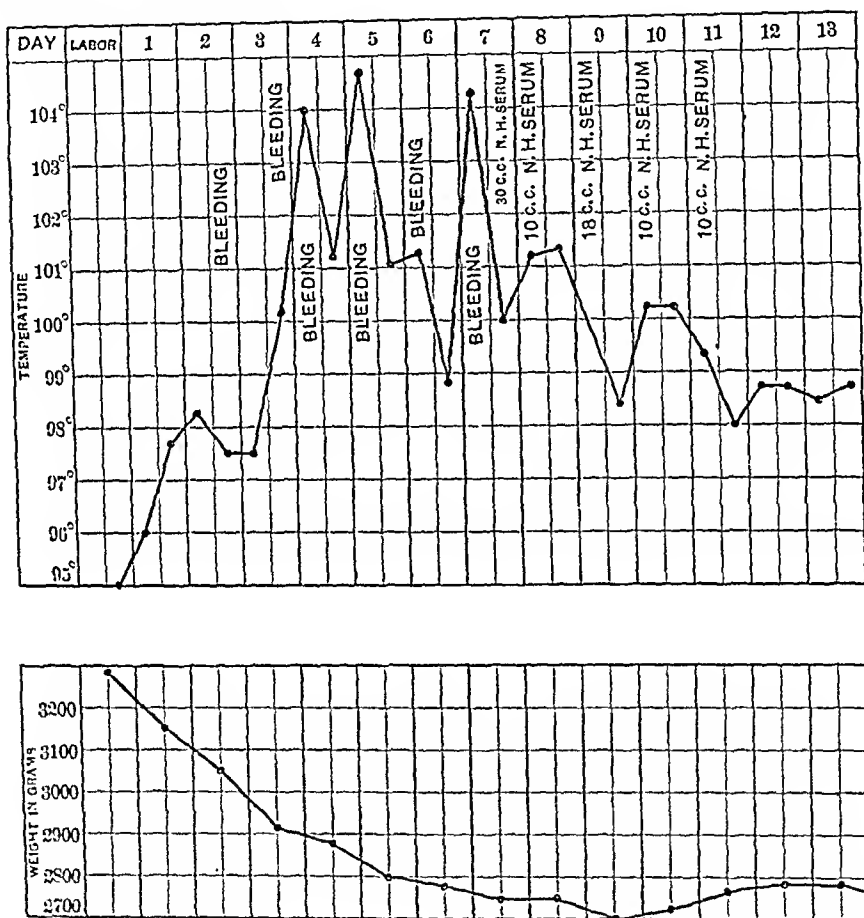


FIG. 4.—Temperature and weight charts of Case IV.

bleeding began, 30 c.c.; on the eighth day, 10 c.c.; on the ninth day, 18 c.c.; on the tenth day, 10 c.c.; on the eleventh day, 10 c.c.; that is, a total, 78 c.c. in five days (Fig. 4). Immediately after administering the serum the temperature, which on the fourth, fifth, and seventh days had been  $104^{\circ}$  to  $104.6^{\circ}$ , subsided rapidly to normal, and the weight, which had declined 550 grams, began slowly to rise. This baby had no more bleeding, but was subject to attacks of cyanosis. It had also a rotary nystagmus. On the fifty-sixth day it died, and autopsy showed the cause

to be a persistent atelectasis of the lungs involving their posterior half. None of the tissues showed any sign of hemorrhage.

CASE V.—First child; male; full term; normal labor. On the third day blood began oozing from the cord at its junction with the skin, from the foreskin, and there was copious bleeding from the nose. The stools were black, showing altered blood. A single injection of 10 c.c. of normal human serum was given, and within six hours the bleeding ceased and the stools on the following day were normal. There was no more bleeding from this baby (Fig. 5).

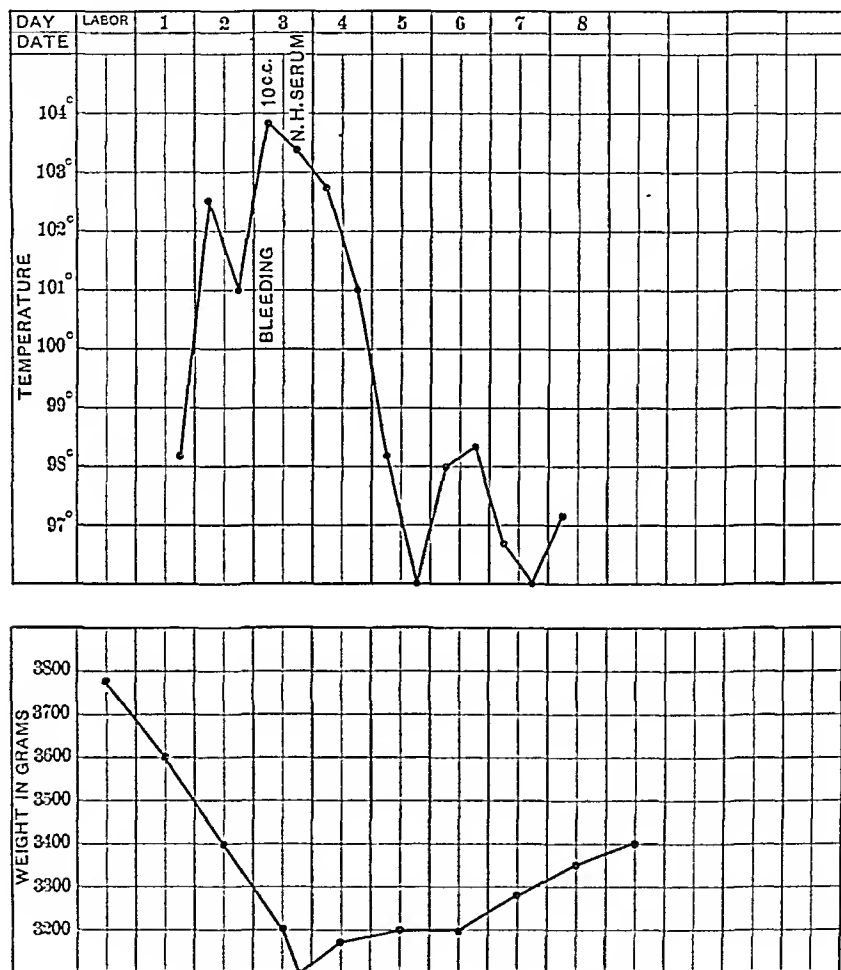


FIG. 5.—Temperature and weight charts of Case V.

CASE VI.—First child; full term; female; normal labor. On the second day it began bleeding from the nose. On the third day it bled from nose and cord, and a large hematoma appeared on the back of the head and neck which extended from ear to ear. There were also subcutaneous bleedings on the right side of the thorax, and slight

jaundice appeared. On the fourth day there was bleeding from the nose and gums and blood was passed in the stools. The hemorrhage in the neck increased, and fresh ones appeared on the scalp and right wrist. On the fifth day slight bleeding from the nose; one spot was noticed on the right knee and left elbow. Normal human serum was injected as follows: On the fourth day, two days after bleeding began, 35 c.c. in three doses; on the fifth day, 20 c.c. in two doses; on the sixth day, 29 c.c. in two doses; on the seventh day, 27 c.c.; on the eighth day, 12 c.c.; total, 123 c.c. in five days (Fig. 6). There was no more bleeding after the fifth day, and the child was discharged on the thirteenth day normal.

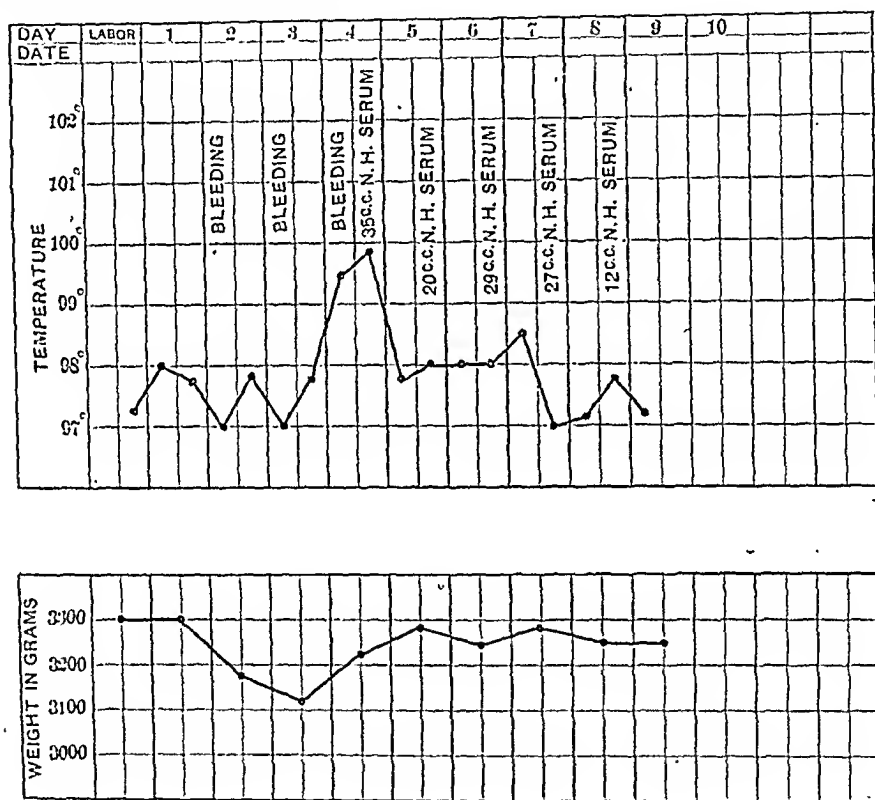


FIG. 6.—Temperature and weight charts of Case VI.

CASE VII.—First child; female; full term; normal labor. Bleeding from the cord and rectum began on the fourth day. On the fifth day bleeding from the vagina and rectum, and two subcutaneous hemorrhages appeared on the left side of the thorax. On the sixth day profuse bleeding from the cord and slight bleeding from the rectum. There was no bleeding on the seventh and eighth days, and no serum was administered in consequence. On the ninth day there was vomiting of blood and slight bleeding from the rectum. On the tenth day profuse bleeding from the cord, vomiting of blood, and bleeding from the rectum, two subcutaneous hemorrhages on

the right side of the thorax, and others on the elbows and on the back. No further bleeding after the tenth day. Normal human blood serum was administered subcutaneously as follows: On the fifth day, one day after bleeding began, 10 c.c. in one dose; on the sixth day, 20 c.c. in two doses; on the ninth day, 20 c.c. in two doses; on the tenth day, 10 c.c. in one dose; on the eleventh day, 8 c.c. in one dose; on the twelfth day, 5 c.c. in one dose; on the thirteenth day, 10 c.c. in one dose; total, 83 c.c. in seven days (Fig. 7). The bleeding in each attack was controlled on the second day. This chart illus-

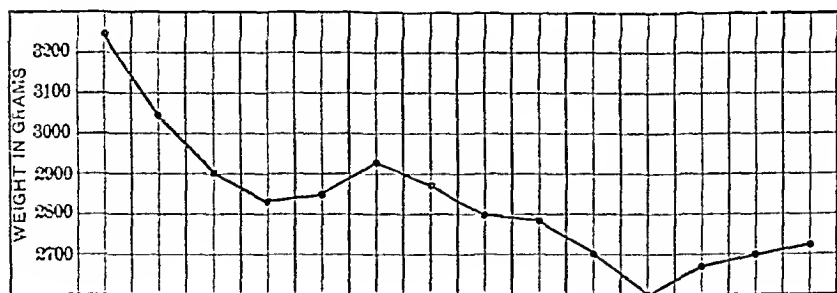
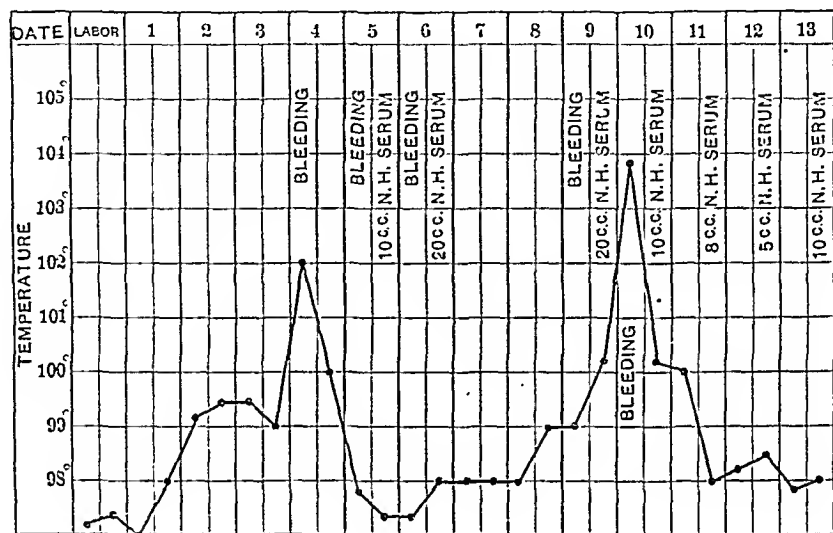


FIG. 7.—Temperature and weight charts of Case VII.

trates twice the manner in which the temperature and weight curves diverge during the bleeding, and how they approach each other when bleeding stops.

CASE VIII.—First child; male; full term; normal labor. On the third day began bleeding from the mouth and rectum. On the fourth day profuse bleeding from the mouth, nose, rectum, and under the skin covering the left scapula. On the fifth day bleeding continued. No bleeding on the sixth day. On the seventh day bleeding from the rectum. No bleeding after the seventh day. Normal human blood

serum was injected subcutaneously as follows: On the sixth day, three days after bleeding began, 7 c.c. in one dose; on the seventh day, 9 c.c. in one dose; total, 16 c.c. in two days (Fig. 8).

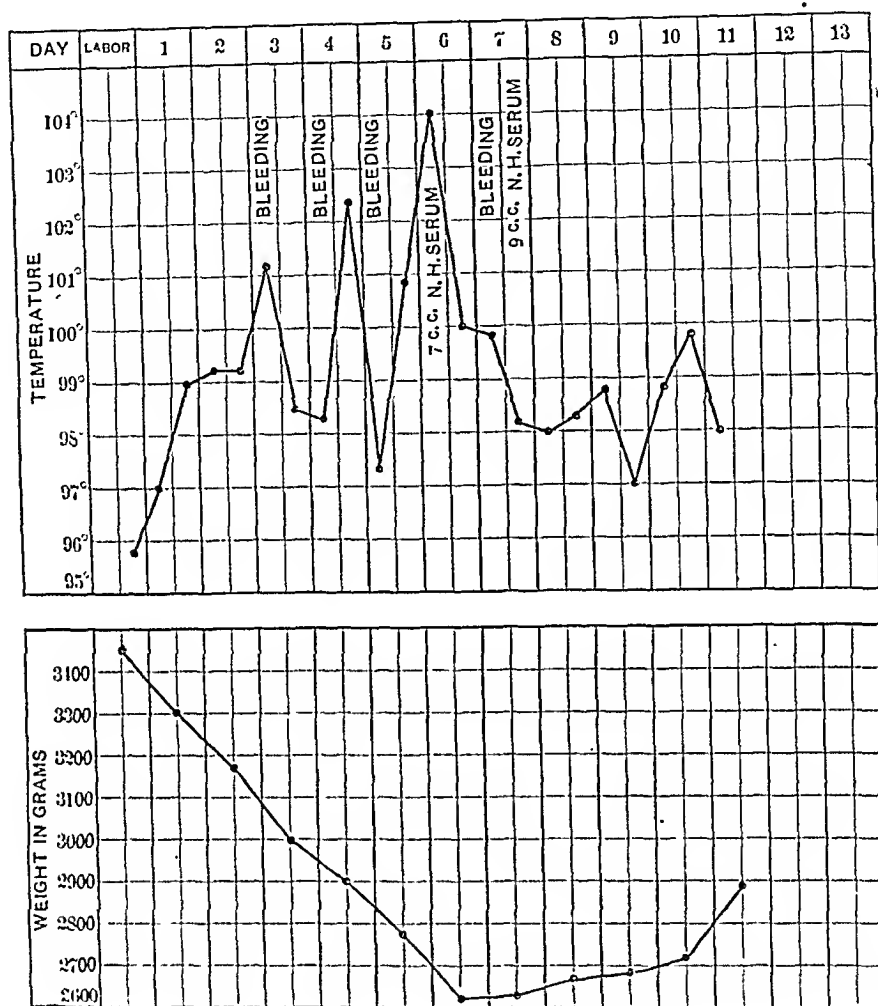


FIG. 8.—Temperature and weight charts of Case VIII.

CASE IX.—First child; full term; male. Mother had a post-partum hemorrhage. At 4 A.M. on the fourth day it had a large hemorrhage from the bowel and vomited blood-stained fluid. At 4.30 A.M. had very profuse hemorrhage from the bowel and vomited small amount of blood. At 10.30 A.M. bleeding from the rectum and vomiting of a small amount of blood. At 11 A.M. hemorrhage from the rectum, and small amount of blood vomited. Baby was very weak, not able to cry out when injected. Pale and jaundiced, waxy looking. The house physician said baby had lost half its blood. At 2.15 P.M. small hemorrhage from the rectum; 3.00 P.M., severe hemorrhage from the rectum; 7 P.M., small amount of slightly blood-stained vomitus, small blood clots in the feces; 10.30 P.M., blood clots in the



stools, slight hemorrhage from the nose, mouth, and rectum. March 23, the fifth day, 8 A.M., vomited small amount of blood; 10 A.M., large amount of blood from the rectum, which was the last bleeding. Normal human blood serum was injected subcutaneously as follows: On the fourth day, day hemorrhage began, 64 c.c. in six doses; on the fifth day, 65 c.c. in six doses; on the sixth day, 30 c.c. in three doses; on the seventh day, 22 c.c. in two doses; on the eighth day, 28 c.c. in three doses; total, 209 c.c. in five days (Fig. 9).

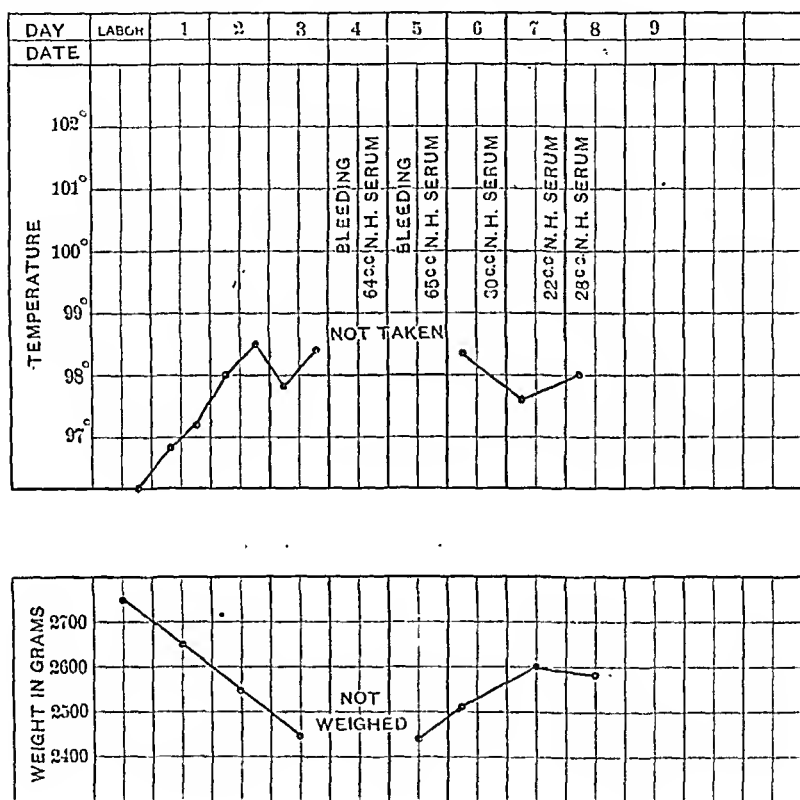


FIG. 9.—Temperature and weight charts of Case IX.

In normal human serum we find an agent that successfully controls hemorrhage in the newborn. I have not gone into the theories as to the causes of these hemorrhages. They are probably due to different factors. In none of the cases could a history of bleeding in the antecedents be obtained. It is possible that some were true cases of hemophilia, while others were due to some infection. In my post-mortem experience I have found, as have others, that the hemorrhages are sometimes due to a bacteremia caused by the streptococcus, staphylococcus, and in some cases a bacillus. I have reason to believe that, even though the bleeding be due to bacteremia, the normal human serum will still be an effective therapeutic agent.

It has been demonstrated so frequently that it is now a matter of common knowledge that fresh normal human blood serum is often bactericidal. If put into the body of a baby in sufficient quantity, and kept moving by the circulation to elimination, it must surely exert this bactericidal effect. I have used it in repeated small and large doses, also in single small and large doses, and am ready to state positively that it never gives serum sickness or causes anaphylaxis in the human subject. On the other hand, it is a perfect form of food, already digested and ready to be taken up and utilized by the tissues and cells of the body, so that without dissipation of energy regeneration may progress with a maximum of efficiency. In many of these babies with bleeding from the gastro-intestinal tract, nourishment from this source is impossible. The alimentary tube is filled with decaying blood, and in most instances there is reversed peristalsis, which militates against digestion, and, added to these, there exists a clouding of the epithelium and considerable desquamation. The food cannot be properly prepared for absorption, and should it be, the circulation is so feeble as to be an obstacle to its removal into the tissues.

When placed under the skin normal human blood serum is quite readily removed from the site of injection. I have seen two ounces completely removed within five minutes by gently massaging the skin over the site of injection while administering the dose. As a further testimonial to the harmless effect of human blood serum, I will refer to some of my work in connection with eclampsia, in which I injected 150 c.c. of serum, removed from an eclamptic patient by venesection, after her twentieth convulsion, into a normal adult, within twenty-four hours, without the slightest noticeable effect, either subjectively or objectively. This patient died of her eclampsia shortly after the venesection.

It may be that the hemorrhage is partly and in some cases entirely controlled by the nutritive effect on the body tissues of the infant. In others it is possible that a thrombokinase is supplied, as suggested by Kottman and Lidsky, who obtained it from animal sera and from the filtrate of the chopped and soaked rabbit livers which they applied locally to check hemorrhages about the cord.

As to the dose of serum to be used in any given case, it should be said that this depends upon the urgency of the case. One is apt to err on the side of too small doses. It is advisable to begin with at least 10 c.c., and repeat three times per day if the infant is bleeding only moderately. In severe cases it should be given every two hours, and in larger quantities if necessary. It is very important to begin the treatment at the first indication of bleeding, however apparently insignificant. Slight bleeding of the cord may be accompanied by fatal internal hemorrhage if not stopped immediately.

The blood is very easily collected. The apparatus (Fig. 10) I have devised consists of a rubber cork through which are two perfora-

tions. Through one perforation is fitted a U-shaped glass tube, to the outer end of which is attached, by means of a piece of rubber tubing, a short aspirating needle having a No. 19 caliber. The needle is cotton-plugged into a small test-tube, in which it is sterilized. Through the other perforation is inserted a fusiform glass tube containing cotton to prevent contaminating the contents of the flask. A small suction tube is placed on this latter for drawing the blood into the flask. The needle is inserted into a vein at the elbow and

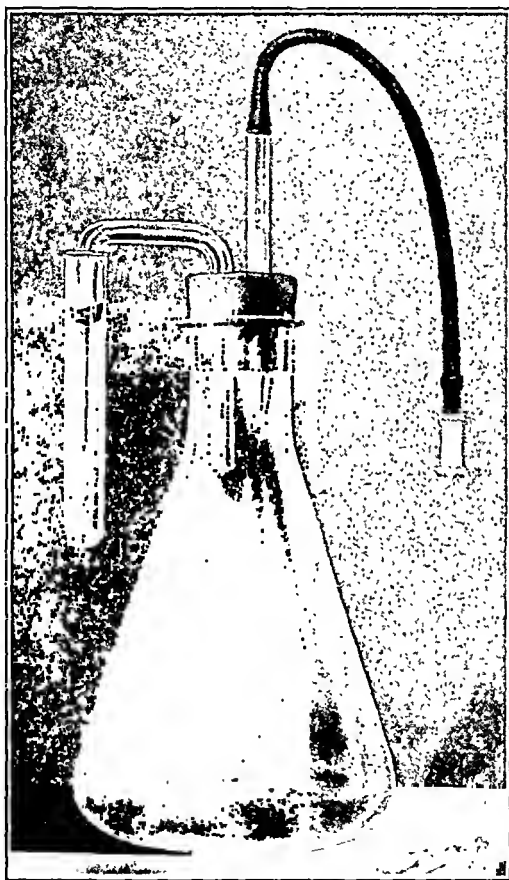


FIG. 10.—Apparatus for collecting the blood serum.

the desired amount of blood withdrawn. The blood is allowed to coagulate in a slanting position in the flask, and the serum is withdrawn as rapidly as it separates, and it is then ready for use.

I have also used subcutaneous injections of normal human blood serum in a case of streptococcemia, with an apparent good effect. The patient's temperature was normal until the third day post-partum, when it rose to 104° F. On the fourth day an intra-uterine culture developed a growth of streptococci and staphylo-

cocci. A blood culture on the sixth day proved sterile. The patient's temperature remained high, so that notwithstanding a negative blood culture she was considered to be suffering with bacteremia. In consequence she was given Hiss' extract of leukocytes on the seventh, ninth, tenth, and eleventh days. The temperature seemed to react well for a few days under this treatment, but finally rose again on the twelfth day to  $104.8^{\circ}$  F., and the patient's condition was very bad. A second blood culture, made on the tenth day postpartum, developed a pure growth of streptococci.

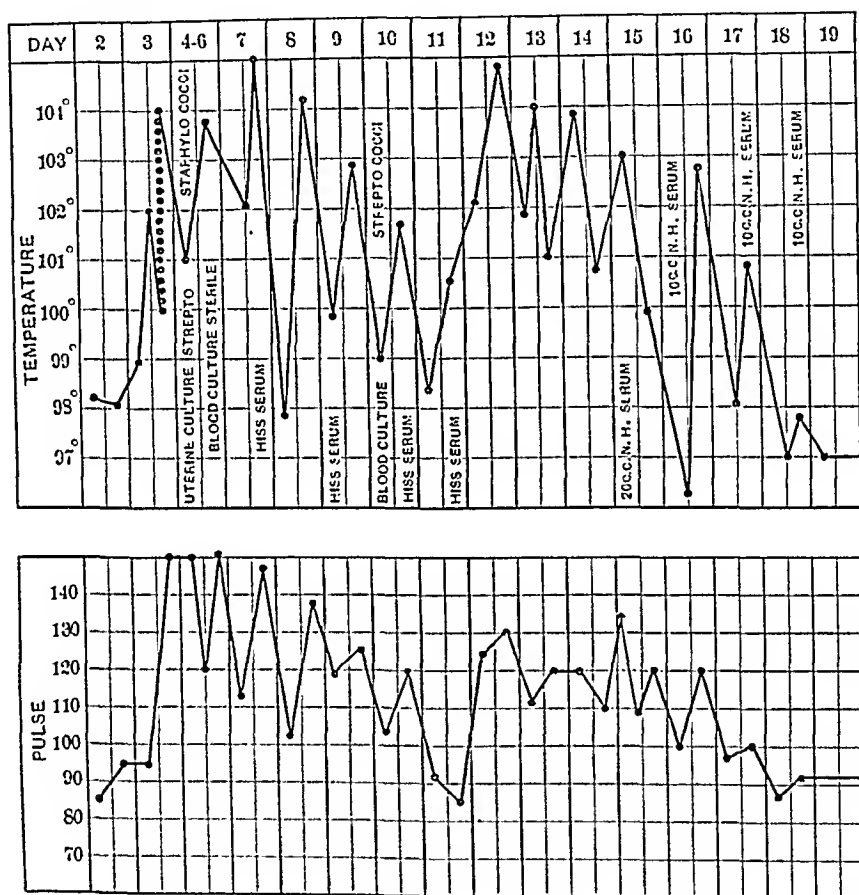


FIG. 11.—The temperature curve and the pulse rate in a case of streptococcemia.

The patient was considered in a hopeless condition from the twelfth to the fifteenth day. On the fifteenth day she received 20 c.c. of normal human blood serum hypodermically, and on the sixteenth, seventeenth, and eighteenth days each 10 c.c. She had no rise of temperature after the nineteenth day. A blood culture made on the twenty-seventh day developed no growth of organisms. The patient was dismissed from the hospital in a normal condition. Fig. 11 illustrates the temperature curve and the pulse rate in this case.

Normal human blood serum administered hypodermically to tuberculous individuals gives excellent results. According to Wright, normal human blood serum contains more opsonin than that of a tuberculous person, and it may be through this property, causing more complete phagocytosis, that the benefit in this condition is derived.

Normal human blood serum has a broader field of application than in the cases herewith mentioned. By means of work now in progress I hope to demonstrate its value in other conditions.

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## THE METABOLISM OF MYASTHENIA GRAVIS, WITH A SUGGESTION REGARDING TREATMENT.

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THROUGH the kindness of Dr. W. G. Spiller, an opportunity has presented for the study of the metabolism in a case of myasthenia gravis.

The subject of myasthenia has received attention, in great degree, from neurologists alone, and though the clinical aspects of the disease have been known for a long time, little has been adduced to date regarding the etiology or pathology. It would seem, in view of these facts, that, except for the great rarity of the disease, attempts would have been made to approach it through other channels; but reference to the literature shows that, with few exceptions, this has not been the case.

For example, in his *Metabolism and Practical Medicine*, von Noorden devotes but one page to the question of myasthenia in general, mentioning the work of Kauffmann, who has investigated myasthenia gravis, more especially in connection with the effect of fatigue upon the nitrogenous metabolism. Kauffmann concludes that with the appearance of fatigue there is a diminution in the output of urea coinciding with an increase in the output of ammonia. He regards this as indicative of an acid intoxication, and ascribes to lactic acid the poisonous role. Lactic acid was found in large quantities in the urine on the days of work, as well as in the blood serum. In Kauffmann's case, as well as in two others reported by Mohr and Boldt, the liver was diseased, and, according to von Noorden, it seems as if the appearance of the myasthenia coincided with the extent of the intermediary products of metabolism.

Perhaps the most significant work on this subject is that of Spriggs, who has investigated the nitrogenous metabolism and the creatinin output in a variety of cases of muscular loss of function.

Spriggs finds that there is a decrease of creatinin in proportion to the decrease of muscle bulk; and that this holds true, though to a less degree, in myasthenia gravis, in which condition, however, there is, of course, little decrease of muscle volume.

When the case now under discussion was first considered with a view to chemical study, general metabolic investigations of the above nature were contemplated on the basis of there having been so little attempted in this connection; but at the suggestion of Dr. D. L. Edsall there were included examinations of the calcium and magnesium metabolism, the former of which afforded the findings of most interest.

Jacques Loeb and his associates showed a few years ago, that certain agents, when injected into the economy, cause precipitation in an insoluble form of the body calcium and produce a condition of muscular spasm. This condition could be induced by him with all the alkaline earths, except barium, and could be relieved by agents which induce the re-solution of the precipitated calcium salts or by a further injection of calcium. Meltzer and Auer have shown that rigor mortis is hastened by the injection of calcium, and under certain conditions, of magnesium salts as well; and have also called attention to the great toxicity of magnesium salts when injected into animals, even in minimal amounts. They have shown, furthermore, that there exists between calcium and magnesium an apparent antagonism, whereby animals rendered nearly moribund by magnesium can be resuscitated immediately by minimal injections of calcium.

In somewhat the same line the work of MacCallum, Voegtlin, and Halstead indicates that there exists an intimate relation between tetany and calcium metabolism. In persons the subject of extirpation of the thyroid for goitre, in whom the parathyroids have also been inadvertently removed, and in dogs in which this procedure has been experimentally performed, there occurs a loss of calcium in the urine and feces. The muscle spasm, increased respiration, and other phenomena characteristic of tetany, however, which follow upon removal of the parathyroids, can be controlled and indeed prevented by the administration of calcium salts in amounts sufficient to compensate somewhat for the loss sustained.

Such observations as the above rendered reasonable the investigation of the calcium and magnesium metabolism in myasthenia gravis in the hope of observing some relation between it and the perverted muscular functions of that condition.

The case under observation was that of an extremely intelligent man, aged about fifty-five years, presenting well-advanced features of the disease. His previous history is without special significance,

and the course of the disease need be mentioned only in so far as to state that it was in some slight degree amenable to diet and hygienic treatment. The intelligence of the patient and his coöperative efforts made possible accurate study upon him, and the subjective evidence advanced by him has been of value throughout, as an index of his progress for better or worse.

He was placed for ten days upon a metabolic diet whose content in the various features investigated either was known or could be easily determined. The features investigated were the total nitrogen, ammonia, creatinin, calcium, and magnesium, all of which were determined in the urine; while the feces were examined for total nitrogen, calcium, and magnesium. Articles of his diet in which the calcium and magnesium content were not known, were submitted to similar investigations.

The methods adopted were the Kjeldahl in the determination of nitrogen and Folin's colorimetric method in the determination of creatinin. The calcium was determined as oxide, after precipitation by ammonium oxalate and subsequent ignition; the magnesium, as oxide, after precipitation with ammonia from the calcium filtrate and subsequent ignition. During the experiment the patient was maintained, as far as possible, under the same circumstances as those under which he had been living just prior to it.

Under the conditions of the dietary administered the patient did well. The determination of the nitrogen balance over a period of six days of the seven days studied showed a nitrogen retention of about 16 grams (16.6117). In this period of six days, however, the calcium metabolism not only failed to keep pace with the nitrogen retention, but did not even maintain an equilibrium, showing, indeed, an actual loss amounting to more than 8 grams (8.4888).

Investigation of the magnesium metabolism showed no apparent departure from the normal. The ammonia output was apparently also well within the limits of health, and no indication of an acid intoxication could be induced therefrom.

Folin's observations have suggested that the creatinin output in any individual is a constant, independent of muscular exercise. Shaffer believes that in pathological subjects the creatinin is usually low, although the creatinin coefficient ( $\frac{\text{K}}{\text{S}}$  per kilo body weight) shows a direct parallelism with the muscular efficiency of the individual; and indicates, furthermore, some special process of normal metabolism taking place largely, if not wholly, in the muscles. The investigations of Spriggs on the creatinin output in several of the primary myopathies, in myasthenia gravis, myotonia congenita, and tabes dorsalis, essentially corroborate this finding, and this worker believes creatinin to be a product of the internal structural metabolism of muscle and not of its contraction.

In a normal individual, Spriggs found the output of creatinin nitrogen expressed in percentage of total urinary nitrogen to be

3.9 per cent. In his series of pathological cases, the creatinin nitrogen as percentage of total nitrogen was as follows:

Normal woman . . . . .	3.9
Progressive muscular dystrophy (boy of 15½ yrs.) . . . . .	0.8
Progressive muscular dystrophy . . . . .	1.7
Tetanus . . . . .	4.0
Tetanus . . . . .	2.2
Spastic paraplegia . . . . .	3.7
Spastic paraplegia (dementia paralytica) . . . . .	4.2
Myasthenia gravis . . . . .	3.0
Amyotonia congenita (boy of 4½ yrs.) . . . . .	0.3
Healthy boy (4½ yrs.) . . . . .	1.0
Locomotor ataxia . . . . .	3.9

The present case showed an average daily output of creatinin of 0.59155 gram, which is slightly below the low limit of excretion in health and also below the figures in Sprigg's case of myasthenia (0.689 gram). Expressed in terms of creatinin nitrogen as percentage of the total urinary nitrogen, however, the output was only 1.67, which is considerably lower than the same quotient in the case just mentioned.

Spriggs deduces from his work that in myasthenia gravis there is a diminution in the creatinin output which should be taken to indicate a connection between the excretion of creatin and muscular function apart from bulk. The present case gives color to this view, and shows, further, that the decrease may be even more marked than that which his case showed, and, indeed, sometimes almost as great as occurs in primary myopathies with loss of muscle substance.

This would seem to suggest that myasthenia gravis is a disease of disturbed internal muscular metabolism *per se*. This finding is peculiarly in consonance with the observed loss of calcium; which element is, as above stated, in close connection with the functions of muscular activity. The relation seems to be more than accidental, and calls for further investigation.

As far as can be ascertained this study forms the only attempt at a determination of the calcium metabolism in myasthenia gravis; and while one case affords insufficient grounds for positive conclusions, it is at least suggestive that, in view of the very intimate relation existing between some of the alkaline earths and muscular activities, there should be observed in this instance so distinct a loss of calcium salts. The patient has remained under the observation of Dr. W. G. Spiller, who has administered calcium lactate over a considerable period of time. Other remedial measures have been ordered, including the use of strychnine; but whether because of the calcium administered or by way of coincidence alone, the patient has markedly improved in the course of the year and a half since the observations above mentioned, and the establishment of the calcium therapy. Remissions of long periods have been reported by several observers in the course of myasthenia gravis, but, at least, they are



rare, and it may well be that we have in this definite indication of disturbed metabolism a clue to practical therapy in this disease.<sup>1</sup>

Through the kindness of Dr. Spiller, opportunity has been afforded for the examination of another case of myasthenia gravis with the same objects in view; but the patient was too refractory to allow of proper control of her diet, and conclusions based upon this study would be unwarranted, except in so far as to state that the results suggested no radical departure from the conditions above described.

**CONCLUSIONS.** The above study indicates that in myasthenia gravis there may be marked loss of calcium by the tissues even under circumstances of marked nitrogen retention.

The creatinin output in myasthenia gravis may be reduced to a point below normal; the output of creatinin nitrogen expressed in percentage of the total urinary nitrogen may be almost as low as that seen in conditions of true muscular wasting.

These facts taken together form a reasonable basis for belief that myasthenia gravis is a disease of deranged muscular metabolism, and that one at least of these two factors (that is, the loss of calcium) may stand in such a causal relationship as to indicate the therapeutic administration of that element.

I wish to express my great obligation to Dr. W. G. Spiller for the opportunity of studying the case, and also to Dr. D. L. Edsall for his suggestions and assistance during the course of the determinations.

Day.	Amount c.c.	Creatinin.	Creatinin N. as per cent. of total urinary N.	Total N. in urine.	NH <sub>3</sub> .	NH <sub>3</sub> N. as per cent. of total urinary N.	Ca.	Mg.
	c.c.	Grams.	Per cent.	Grams.	Grams.	Per cent.	Grams.	Grams.
24	1550	0.6448	1.99	11.8876	1.0961	5.47	0.4550	0.2859
25	1390	0.6258	1.70	13.4848	0.7235	4.41	0.5045	0.2533
26	1415	0.5387	1.567	12.6266	0.5522	3.60	0.5515	0.1714
27	760	0.5476	1.840	10.9318	0.6610	4.055	0.4371	0.2639
28	1235	0.4281	1.23	12.7350	0.8500	5.41	0.4379	0.2906
29	1645	0.6654	1.55	15.7514	1.0322	5.39	0.5433	0.2605
30	1906	0.7437	2.12	12.8532	0.6566	4.207	0.5862	0.2840
Urinary totals	3.5493	Av., 1.668	78.3828	4.4755	Av., 4.5116	3.0714	1.5237	

Ca. in feces . . . . .	18.6051 grams
Mg. in feces . . . . .	0.7257 gram
N. in feces . . . . .	4.9156 grams

<sup>1</sup> In a later report the patient says that for the first time since his illness began he feels that his complete recovery is possible and not far distant.

Sum total of output:	
Creatinin . . . . .	3.5493 grams
Total N. . . . .	83.2984 grams
Total NH <sub>3</sub> . . . . .	4.4755 grams
Total Ca. . . . .	21.6765 grams
Total Mg. . . . .	2.2514 grams

Average diet<sup>2</sup> consisted of:

Breakfast:	
Eggs. . . . .	90 grams
Bread . . . . .	50 grams
Milk . . . . .	420 c.c.
Butter (for day). . . . .	40 grams

Dinner:	
Eggs. . . . .	90 grams
Bread . . . . .	50 grams
Milk . . . . .	420 c.c.
Rice . . . . .	30 grams

Supper:	
Eggs. . . . .	90 grams
Bread. . . . .	50 grams
Milk . . . . .	420 c.c.
Apples . . . . .	130 grams
Sugar . . . . .	32 grams
Salt . . . . .	5 grams

Total food consumed in six days:	
Eggs . . . . .	1719 grams
Bread . . . . .	1050 grams
Milk . . . . .	8340 c.c.
Rice . . . . .	210 grams
Apples . . . . .	910 grams
Butter . . . . .	280 grams
Salt . . . . .	30 grams
Sugar . . . . .	210 grams

## Total grams of Ca. and N. in intake of food:

Ca. . . . .	13.1877 grams
N. . . . .	99.9101 grams
Positive N. balance of <sup>3</sup> . . . . .	16.6117 grams
Negative Ca. balance of . . . . .	8.8888 grams

<sup>2</sup> In order to save space the diet tables are not given entire, but the balance was made up on the actual totals and not on the basis of an average day. The percentage content in Ca. and N. of eggs, bread, milk, rice, and butter is taken from "A Contribution to the Chemical Pathology of Acromegaly," by Edsall and Miller, University of Pennsylvania Medical Bulletin, vol. xvi, p. 143.

<sup>3</sup> The balance was made up on the last six days, as there was some discrepancy in the diet figures for the first day. As a matter of fact, however, this discrepancy could be safely disregarded and the amount ingested for that day assumed as practically identical with those following, as the figures are in perfect accord. This makes the metabolism studies cover, essentially, a period of seven days, one more than that actually considered. The magnesium output was so obviously within normal limits that a balance was not computed.

## THE TREATMENT OF SPASTICITY AND ATHETOSIS BY RESECTION OF THE POSTERIOR SPINAL ROOTS.<sup>1</sup>

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CASES of spasticity are very numerous, and in some instances the spasticity is far greater than the motor palsy; indeed, if the implication of the pyramidal tract be slight, the spasticity, in the opinion of some, is greater than when the degeneration is intense. Spasticity is affected by various conditions. Sensory irritation, such as cold, faradic electricity, handling of the body, or voluntary movement increases the spasticity; and sleep may diminish it; so that spasticity may be less in the morning than in the evening. These effects are produced through the peripheral nerves.

Irritation of peripheral sensory fibers, as in joint disease, may increase the tonus and cause contracture. It is common to find the tendon reflexes exaggerated in the wasted limb in arthritic muscular atrophy.

Athetosis is essentially a form of spasticity, differing from ordinary spasticity chiefly in the varying degree of tonicity in the different muscles. An athetoid limb is one necessarily spastic, and first one group of muscles, then another, exhibits a predominance of the spasticity. This view has been shared recently by Schwab and Allison;<sup>2</sup> they state that athetosis and spastic conditions of organic origin are essentially similar processes; that athetoid movements may be regarded as variants of permanent tonic spasticities.

In order that we may have clearly in mind the rationale of the method of treating spasticity by resection of the posterior roots, it may be well to give at this juncture an elementary sketch of the chief factors concerned in spasticity.

Muscular tonus depends on the integrity of the peripheral sensory nerve fibers, of the posterior roots, of the cells of the anterior horns, and of the peripheral motor nerve fibers. Fibers pass through the brain and cord and exert a controlling influence over the spinal reflexes. These fibers have an inhibitory effect, and act as a damper on the spinal reflexes. In contrast with these are possibly other fibers whose function is to accelerate the tonus, "bahnende" fibers of the German writers. It may be partly from irritation of the latter that in slight lesions of the pyramidal tracts tonicity may be greater than in complete destruction of these tracts.

<sup>1</sup> A lecture delivered at the University of Pennsylvania during "Home Coming" week, March 29, 1910.

<sup>2</sup> *Journal of Nervous and Mental Disease*, August, 1909; *Journal of the American Medical Association*, February 12, 1910, p. 551.

The inhibitory effect of the cerebrum on the spinal reflexes is probably accomplished through the pyramidal tract. Afferent impulses are passing constantly from all parts of the body below the head to the spinal cord, and exert an influence on the cells of the anterior horns of the spinal cord, by means of which motor impulses are sent out to the muscles. It is, indeed, fortunate for us that many of these reflex acts do not enter our consciousness. When standing in a rapidly moving car we may be engaged in reading, and yet are constantly and unconsciously altering the tonicity of opposing groups of muscles. A wooden figure of the same proportions as the human body placed in a similar position would soon fall over. During life our muscles are constantly in a state of tonicity suitable for the various functions they are called upon to discharge, but in disease this condition of well-adjusted tonicity may be altered. A soldier standing "at attention," as Strümpell has said, exhibits the most perfect movement.

When some lesion damages the pyramidal tract the inhibition of the brain is removed and the spinal reflexes are left without control. The desideratum would be the restoration of the pyramidal tract, but that manifestly is impossible. The next best thing is to remove some of the afferent peripheral impulses, so that the cells of the anterior horns may not be kept in a state of overexcitement. It is possible that in lesions of the pyramidal tract the excessive tonicity is caused by the cerebellum, and theoretically it might be desirable to operate so as to influence the action of the cerebellar nuclei. An operation may be devised some day with this end in view, although at present it does not seem possible, and yet in 1905 the proposal of division of the posterior roots to influence spasticity met no response.

In this connection I quote from J. S. Risien Russell's Lettsomian Lectures:<sup>3</sup> "As sensation does not accrue as a result of all peripheral stimuli which evoke a central (reflex) action, Sherrington adopts 'receptor' as the neutral term to apply to the peripheral apparatus, which receives the stimulation. He points out that there are two main fields of distribution of the receptor organs—a *surface field*, which is situated at the surface layer of the organism, but external and internal, which he speaks of as exteroceptive and interoceptive respectively; and a *deep field*, which is situated in the tissues of the organism beneath the surface layer, which he designates proprioceptive. The stimulations which occur in the deep field are traceable to actions of the organism itself, as opposed to stimuli received from without. Hence the term 'proprioceptor,' which he has applied to these stimuli, which are brought about largely, as he says, through the agency of mass, with its mechanical consequences of weight and inertia, and also largely through mechanical strains and alterations of pressure, resulting from contractions and relaxa-

<sup>3</sup> British Medical Journal, February 19, 1910, p. 425.

tions of muscles. Among the functions subserved by the receptors of the proprioceptive, or deep field, is that of maintaining a state of tonic reaction in the skeletal muscles, which Sherrington regards as concerned with the maintenance of attitude. . . .

"Bouché has determined that fits induced by intravenous injection of absinthe in an animal deprived of one cerebral hemisphere were clonic and mainly flexor in type from the intact cerebral hemisphere, whereas the fit on the other side was tonic and chiefly extensor. Section of the mesencephalon during the fits abolished the clonic discharges, and only allowed the tonic to continue. Even more striking are the results of Leonard Hill, who was able to alter the character of the fit from tonic to clonic at will, according as he interrupted the arterial supply to the cerebrum by clamping the vessels or allowed the blood charged with absinthe to reach the brain. . . .

"Sherrington has shown that removal of the cerebrum results in what he speaks of as decerebrate rigidity, which fully accords with Dr. Jackson's view of cerebellar influx. Moreover, he found that this rigidity could be abolished, and was replaced by flaccidity in the homolateral limbs on hemisection of the spinal cord in the cervical region, which makes it evident that tonus is derived from the mesencephalon or cerebellum. Sir Victor Horsley, acting on Dr. Jackson's suggestion, divided the mesencephalon at the level of the intercollicular groove, and thus allowed of decerebrate rigidity appearing. Removal of successive sections of the cerebellar cortex produced no appreciable effect on the hypertonus until the sections involved the intrinsic and paracerebellar nuclei [nuclei of Deiters and von Bechterew]. A large horizontal lesion, separating the dorsal half of the cerebellar cortex without involving the nuclei, was also made three weeks before the division of the mesencephalon, again without any appreciable effect on the decerebrate rigidity which resulted in these animals, as compared with that which obtained when a similar section of the midbrain was performed in normal animals. Thiele, in his researches undertaken with a view to determine the source from which the hypertonus which constitutes Sherrington's decerebrate rigidity is derived, found that the chief source of this energy was at the level of the paracerebellar nuclei. Successive lesions of the mesencephalon, commencing in front and proceeding caudalward, failed to affect the decerebrate rigidity until the nuclei were reached. The experimental evidence is thus convincing, both as proving that the nuclear region of the cerebellar complex is the source of the energy, which constitutes the cerebellar influx, and as thus confirming the view enunciated by Dr. Jackson more than thirty years ago. . . .

"All the facts that have been established in regard to the cerebellum are in accord with a view that its cortex is concerned with the reception of afferent impressions which are derived from deeper structures like the muscles and joints, as well as those which the

organ receives from the labyrinth, and that efferent impulses are thus evoked from its muscles, which are responsible for that degree of tonus in the general musculature of the organism which is essential for the maintenance of attitude, and which makes it possible for coördinated movements to be executed."

These important statements show that tonicity of muscles depends on the cerebellum, and probably on its nuclei, and less so on the cerebrum. The connections of peripheral afferent fibers with the cerebellum is by means of the posterior roots. It is probable that in excessive tonicity destruction of the cerebellar nuclei would produce flaccidity. By cutting the posterior roots from a spastic limb we weaken or destroy this spasticity by removing the impulses to the cerebellum, on which organ it depends, and therefore the operation has a logical basis. Were we in a position to increase the cerebral inhibition over the motor tracts, we should not resort to resection of the posterior roots.

Various attempts have been made to overcome spasticity. In a paper read in 1905 with Dr. Frazier<sup>4</sup> before the New York Neurological Society on the treatment of cerebral palsies and athetosis, nerve anastomosis, was discussed. At that time I recommended the resection of the posterior roots for the relief of spasticity and athetosis, but the idea was so novel it called forth no discussion, and, receiving no encouragement, I hesitated to advise further an operation that seemed too much like an experiment on man, and one not without danger. We therefore contented ourselves with an attempt to relieve spasticity and athetosis by anastomosis of one peripheral nerve with another, hoping that we might satisfactorily diminish afferent impulses, although we knew that we must diminish efferent impulses, but felt that sufficient efferent motor impulses would be left for fair discharge of function. The results seemed at first very promising. The most extreme spasticity and athetosis yielded to this treatment, but the young man on whom the operation was performed deserted the hospital and withdrew himself from our observation. When we saw him again, some three years later, athetosis in the operated limbs had almost disappeared, but contracture had become pronounced and interfered greatly with voluntary motion.

An attempt similar to ours has been made by Nutt<sup>5</sup> recently. This author believes that much may be gained by cerebral rest. His method differs from ours only in uniting the cut ends of the same nerve instead of uniting the cut ends of different nerves.

Schwab and Allison have proposed another method of treatment for the relief of spasticity. Their method is described as follows: "We have been led to devise a method which we shall refer to as muscle group isolation. This implies the isolation of the muscle

<sup>4</sup> Journal of Nervous and Mental Disease, May, 1905; American Journal of the Medical Sciences, March 1906; University of Pennsylvania Medical Bulletin, January, 1910, p. 314.

<sup>5</sup> American Journal of Orthopedic Surgery, November, 1909, p. 151.

or the group of muscles which are at fault in the production of contracture, deformity, or athetosis. It is made effective by cutting off from the central nervous system the connection along which the abnormal impulses, active in causing spasticity or athetosis, are transmitted. This is done by a direct attack on the nerve itself, by isolating it, and injecting it with an alcoholic solution. There has resulted in the cases to be described an immediate paralysis of the physiologically stronger group of muscles without interfering with the free muscular use of the antagonists. At this point physiological exercises planned to further strengthen the antagonist may be used."

Schwab and Allison have recently (February 12, 1910) stated that they regard their method as holding considerable promise of relief. They have not attempted to cure spasticity by alcoholic injections into the peripheral nerves. They believe that by their method the peripheral pathway of the spastic impulses being temporarily blocked, their return in the original sum might be lessened.

More promising than any other method for the relief of spasticity has seemed to me for some five years the resection of posterior roots innervating the spastic limbs. He who studies disease probably has many indications justifying this operation. So far back as 1893 or 1894 I observed return of the patellar reflex in tabes after hemiplegia had occurred. This return of reflex irritability indicated that the degeneration of the posterior lumbar roots in this case of tabes had been sufficient to abolish the reflex, but that enough fibers were retained in the posterior roots to permit a return of this reflex when cerebral inhibition over the spinal reflexes was removed by degeneration of the pyramidal tract. The opposite conditions to those described in this case have been observed repeatedly. When degeneration of the pyramidal tracts has been followed by degeneration of the posterior columns extending well into the lumbar region, in posterolateral sclerosis, spasticity and exaggeration of tendon reflexes have given place to flaccidity and diminution of tendon reflexes.

Unquestionably the first operation for the cure of spasticity by division of the posterior roots was made by O. Foerster's directions.<sup>6</sup> His first paper was published in 1908. He relied on Sherrington's experiments on monkeys, by which it was shown that resection of one or two posterior roots produced no anesthesia, and that the sensation of any cutaneous area depends on three roots, and that not until three adjoining roots are cut does anesthesia occur. As yet satisfactory investigations concerning man are wanting, although it has been demonstrated that division of a single posterior root causes no sensory disturbance. Bruns believes that more than three roots

<sup>6</sup> Zeitschrift für Orthopädische Chirurgie, 1908, xxii, 1 to 3; Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie, 1909, xx, 493.

may supply any cutaneous area. Foerster has never had more than two adjoining roots divided.

For the report that he makes in his second paper he selected two cases of congenital spastic diplegia, one case of tuberculous cervical spondylitis, one case of multiple sclerosis, and one case of hemiplegia. After the operation a certain resistance of the muscles persisted for several weeks in passive movement and extension of the limbs. This resistance he attributes to the pain from the irritation of the posterior roots produced by the cutting. He found at first after the operation that the leg was flexed at the knee and the thigh flexed on the hip, rotated inward, and adducted. This position alters as the cut roots degenerate, as does also the resistance of the muscles in passive movement. In spastic paralysis cutting of tendons or muscles seldom is successful. In some cases tenotomy may be necessary after division of the roots. Foerster recommends that the limbs should be placed in some corrective apparatus after division of the roots, to avoid faulty position.

The Achilles reflex was lost after the operation in Foerster's cases. He attributes this to the cutting of the second sacral and possibly also of the fifth lumbar root. It is not known positively in which posterior roots the Achilles reflex lies, but Foerster places it from his cases in the first and second sacral and possibly fifth lumbar roots.

Tietze<sup>7</sup> says the operation is not very dangerous. He had five cases with one death, and death in this case was by infection from decubitus. Gottstein had two operations and Küttner five operations and no deaths. It is, however, recognized as a major operation. Tietze refers to another fatal case in which collapse occurred before the roots were cut.

Successful cases treated by this means have been reported by Clarke and Taylor,<sup>8</sup> and Taylor has diminished the seriousness of the operation by devising unilateral laminectomy.

Dr. Frazier and I have reported one case in detail in which the results of the surgical treatment have been most satisfactory. Since the publication of that report the improvement in the patient's gait has been marked. He has been receiving systematic training in walking from Dr. Wm. Burdick.

The patient referred to at a previous part of this paper, on whom nerve anastomosis was performed, has also been treated by this method of resection of the posterior roots by Dr. Frazier, and in this case the cervical roots were cut. Improvement in this case also is distinct, but tenotomy may be needed on account of the shortening of the flexor muscles of the elbows.

Resection of posterior roots is useless when paralysis is intense.

In regard to some of the objections made to the treatment, I acknowledge that the operation is serious; had it not been so I

<sup>7</sup> *Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie*, 1909, xx, 559.

<sup>8</sup> *New York Medical Journal*, January 29, 1909, p. 215.



should not have remained contented in 1905 in merely proposing this operation, but because of its seriousness we hesitated to carry out the suggestion. Cortical rest produced by peripheral operations seems to me a condition of little weight in the treatment of spasticity.

The overlap of sensory distributions is considerable, but this does not mean that all the posterior roots of a limb must be cut to lessen spasticity. In the lumbar region the roots at their origin arc near together; and in the cervical region, though not so near as in the lumbar region, they are still close to one another, and therefore exposure of a very large area is not necessary. No one would desire complete sensory paralysis from cutting the posterior roots; a paralysis of this kind would be unnecessary, and would probably cause incoördination and defeat the object of the operation. Indeed, because of the overlapping of root distributions loss of sensation is not likely to occur. Considerable impairment of sensation developed in our first case, but this was probably because the man had had previously great impairment of sensation from his injury, and while sensation had returned, the fibers within the cord were far from normal, and therefore after the resection of certain posterior roots too few afferent fibers were left for the maintenance of sensation. Little or no disturbance of sensation was caused in our second case by extensive resection of posterior cervical roots.

In conclusion, I would say that a means has been devised full of promise for selected cases of spasticity and athetosis, and that these conditions which formerly perplexed and baffled us have in a considerable measure yielded to treatment. Undue enthusiasm is to be deprecated, as bringing the method into disrepute. Cases must be carefully selected, and only those are available in which spasticity is great and weakness is comparatively slight. The association of athetosis need not be a deterring factor, as the strength of a limb often is increased by the excessive muscular action of athetosis. As in every new method, caution is needed, and proper valuation can be placed upon the method only when more experience has been obtained.

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## THE PATHOGENESIS OF THE TOXEMIA OF PREGNANCY.<sup>1</sup>

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It is a curious maladjustment of Nature that places pregnancy among conditions difficult to separate from the pathological. We are accustomed to refer the high morbidity of gestation to the unhygienic influences of modern life, and love to refer to the Indian women

<sup>1</sup> Read at a joint meeting of the Pathological Society of Philadelphia and the Philadelphia Obstetrical Society, February 10, 1910.

who overtook the moving caravans of their tribes after a brief delay for parturition, but history says little about the women who never caught up with the caravan. Today obstetrics in India, China, and Africa deals with the same ponderous process and meets the same formidable hazards as in Europe and America. The comparative study of gestation reveals throughout the animal kingdom a certain lethal tendency reaching its acme in some orders of insects in which ovulation necessarily entails death. Indeed the human family is comparatively fortunate in many of its natural relations to the propagation of the species, while increasing medical intelligence should eventually shield maternity with effective safeguards not provided for the lower animals.

Of the many clinical or more obvious signs of the intrinsic pathology of gestation, some are exhibited by the great majority of gravida, while the notable minority who seem to escape are all liable to the larger accidents of parturition and the puerperal state. Anatomical studies long ago pointed to the kidney as the organ most liable to suffer damage and most responsible for the characteristic grave disorders of gestation. Leyden's "kidney of pregnancy" is firmly established as a very common and in some degree probably constant pathological condition. It consists essentially of a definite, often pronounced grade of fatty degeneration, which forms a background for the more severe lesions which are often encountered in disease, and which include acute degeneration, exudative nephritis, glomerulonephritis, or widespread necrosis, reaching at times almost complete destruction of the organ. In some respects these renal lesions and the associated symptoms are peculiar to pregnancy, and at least in their extent and severity they are not paralleled in any other autotoxic state.

For more than fifty years attention has been directed toward the liver as the probable seat of disease in several of the grave and fatal disorders of pregnancy. I find these indications very clearly apparent in von Frerich's famous work on *Diseases of the Liver*.<sup>2</sup> Here are presented the clinical symptoms and anatomical lesions of acute malignant jaundice, acute yellow atrophy, and eclampsia, with such accuracy and force that the hepatic lesions have never since lost the prominence which his observations helped to give them. It seems to have been the opinion of von Frerichs and Klebs<sup>3</sup> and others that all these diseases with pronounced hepatic lesions were closely related conditions, but in 1896 Jurgens<sup>4</sup> pointed out the specific anatomical changes of the hemorrhagic hepatitis of eclampsia, and he with Lubarsch,<sup>5</sup> Schmorl,<sup>6</sup> and many later writers, have endeavored

<sup>2</sup> *Diseases of the Liver*, Sydenham Soc. Trans., 1860, 192.

<sup>3</sup> Ziegler's Beiträge, 1888, iii, 1.

<sup>4</sup> Fettemboli u. Metastase von Leberzellen bei Eclampsie, Berl. klin. Woch., 1886, 519.

<sup>5</sup> Die Puerperaleclampsie, Erg. d. allg. Path. etc., 1896, I Abt.

<sup>6</sup> Path.-Anatom. Untersuch. über Puerperaleclampsie, Leipzig, 1893, Arch. f. Gyn., 1902, lxx, 504.

to establish a sharp distinction between eclampsia and other autotoxic states. Although it is a rule that auto-intoxications show mild as well as severe forms, there was for many years little tendency to connect the fatal hepatic cases with the milder disorders of pregnancy. The door to progress in this direction was opened by Lindemann,<sup>7</sup> 1892, who in a fatal case of prolonged pernicious vomiting described multiple neuritis and advanced degenerative lesions in the organs, especially in the liver, and referred the vomiting and ptialism to degenerative changes in the central and peripheral nervous systems. In 1895 Eulenberg<sup>8</sup> collected thirty-eight cases of neuritis with hyperemesis, most of which recovered. The toxic nature of hyperemesis was here strongly indicated, as well as its probable association with lesions of the liver. Thus the basis was laid for inculcation of the liver in all the peculiar autotoxic states of gestation. The more thoroughly the organ has been examined the more constant have certain lesions been found to be, so that today one must recognize the liver of pregnancy as well as the characteristic kidney of this supposed physiological condition. In 1885 Roughton<sup>9</sup> pointed out that in normal pregnancy the liver often shows mild grades of just those lesions which appear in pronounced form in the fatal disorders.

According to Hofbauer,<sup>10</sup> 1908, the liver in pregnancy constantly shows in some degree the following alterations: (1) Fatty degeneration of central portions of lobules; (2) limitation of glycogen to the peripheral portions; and (3) bile stasis. These changes, he believes, explain the functional disorders, long recognized by French writers, which consist in diminished capacity to metabolize carbohyrates, a tendency toward glycosuria, and lessened detoxicating power.

The unstable nervous system of the pregnant woman has probably never escaped comment, has been the subject of much curious and some absurd speculation, and even in recent years German obstetrical opinion, led by Ahlfeld<sup>11</sup> and Kaltenbach,<sup>12</sup> was disposed to attribute to this factor the greater share of the disorders and even many of the fatalities of gestation. There is no doubt that the threshold of functional activity of the nervous system is lowered in pregnancy and that this factor greatly influences symptomatology. Blumreich and Zuntz<sup>13</sup> secured interesting experimental evidence in this field when they showed that pregnant rabbits subjected to

<sup>7</sup> *Zur. path. Anat. d. unstillbaren Erbrechen d. Schwangeren*, *Cent. f. allg. Path.*, 1892, iii, 625.

<sup>8</sup> *Ueber puerperale Neuritis u. Polyneuritis*, *Dent. med. Woch.*, 1895, 118, 140.

<sup>9</sup> *Lancet*, 1885, ii, 425.

<sup>10</sup> *Beiträge z. Aetiol. u. z. Klinik d. Graviditätstoxicoesen*, *Zschr. f. Geb. u. Gyn.*, 1907, lxi, 200.

<sup>11</sup> *Hyperemesis gravidarum, Ptyalismus, Hysterie*; *Centrlb. f. Gyn.*, 1891, xv, 329.

<sup>12</sup> *Ueber Hyperemesis grav.*, *Zeitschr. f. Geb. u. Gyn.*, 1891, xxi, 200.

<sup>13</sup> *Exper. u. klin. Beitr. z. Path. d. Eclampsie*, *Arch. f. Gyn.*, 1902, lxx, 737.

repeated light blows on the head responded with convulsive movements far more readily than controls.

Nervous irritability forms a part of the abnormal physiology of gestation, but that any form of intrinsic neurosis can account for the grave disorders of pregnancy is a doctrine always without scientific foundation, and now largely abandoned. An unstable nervous system is the medium of expression of some symptoms of disturbed functions of other organs, but of these disorders of function the nervous system originates none, although aggravating and perpetuating many. There are, thus, as very common changes in what passes as normal pregnancy, lesions in the chief excretory organ, the kidney, in the main organ of metabolism, the liver, and functional instability of the nervous system, the great organ of the expression of symptoms.

Starting from the basis of these essential disturbances of structure and function of the organs, the pronounced clinical forms of the toxemia of pregnancy show striking variations, which tend to impress the observer as wholly different diseases. Ordinary and pernicious vomiting, acute yellow atrophy, malignant jaundice, and eclampsia would seem, superficially, to have little relation to one another. The older writers, however, were inclined to regard eclampsia and yellow atrophy as in some way related, while several French observers were committed to the belief in the autotoxic nature of the chief disorders peculiar to pregnancy, without, however, defining the nature of the relation between them.

Isolated suggestions that many of the milder symptoms were connected with degeneration of the liver were made by Duncan<sup>14</sup> in 1879 and by Roughton in 1885. Before 1894 Davis<sup>15</sup> recognized certain forms of toxemia and based his diagnosis and treatment partly on the low urea ratio and the presence of glucose and acetone in the urine. Allbutt,<sup>16</sup> Bacon,<sup>17</sup> and Schwab<sup>18</sup> discussed the toxic and hepatic origin of pernicious vomiting in 1896. St. Blaise,<sup>19</sup> in 1898, constructed a strong argument for the view that all the mild disorders are the result of functional disturbance of the liver and constitute only a prelude to the eclamptic seizure. He emphasized especially the resemblance between these disorders and those of recognized cases of hepatism, and mentioned the low urea ratio of both conditions. In France, also, Bar<sup>20</sup> and Roger<sup>21</sup> had discussed the significance of the low urea, high ammonia, and the presence of peptones in the urine. In 1903 Whitney and Clapp<sup>22</sup> presented a careful study

<sup>14</sup> Hepatic Diseases in Gyn. and Obstetrics, *Med. Times and Gazette*, 1879, i, 57.

<sup>15</sup> Toxemia of Pregnancy, *AMER. JOUR. MED. SCI.*, 1894, cvii, 147.

<sup>16</sup> *Lancet*, 1897, i, 579.

<sup>17</sup> *AMER. JOUR. MED. SCI.*, 1898, cxv, 683.

<sup>18</sup> De l'auto-intoxication grav. et de ses conséquences, *Arch. gén. de méd.*, 1897, ii, 720.

<sup>19</sup> Les auto-intoxications gravidiques, *Annal. de gyn. et d'obstet.*, 1898, i, 342, 372.

<sup>20</sup> Mercier et Menu, *Traité d'accouch.*, 1897, iii, 703.

<sup>21</sup> Action du Foie sur les poisons, *Thèse de Paris*, 1887.

<sup>22</sup> Urinary Changes in Pregnancy, etc., *Amer. Gynecology*, 1903, iii, 121.

of the urinary nitrogen, pointing out the high proportion of nitrogen precipitable by phosphotungstic acid in eclampsia, and suggested the possibility that this sign might prove of diagnostic value. Prevailing obstetrical opinion, however, persistently ignored the importance of these observations. In 1903 Williams was fully abreast with current views when, in his *Text-book of Obstetrics*, he presented the toxic and hepatic theory merely as worthy of consideration and discussed toxemia and hyperemesis as different conditions. The first definite observation clearly indicating that the ordinary vomiting of pregnancy results from a toxic process which may end in acute yellow atrophy was made by Stone<sup>23</sup> in 1903 in a case studied in the Cornell Laboratory. The general conclusions drawn from this and a series of other cases I presented to the New York Obstetrical Society in 1904,<sup>24</sup> which were to the effect that persistent vomiting, acute yellow atrophy, and eclampsia, are closely related toxic conditions of metabolic and chiefly of hepatic origin, and that chemical analysis of the urinary nitrogen gives indications in support of this view, and should be employed in diagnosis. For three years thereafter Wolf and I<sup>25</sup> endeavored to determine the exact relation between changes in the urinary nitrogen and the diseases in question, publishing the results in 1907.<sup>26</sup> Williams,<sup>27</sup> and Edgar,<sup>28</sup> accepting the toxic theory of origin, employed urinary analyses in many clinical cases, with somewhat different interpretations and varying success. Williams, in 1906, gave a full review of current theories regarding toxemia, and endeavored to establish the urinary ammonia ratio as a safe guide in diagnosis and prognosis. Although his interpretation of the significance of the ammonia ratio was probably too rigid, his observations were of much value in drawing attention to the importance of detailed urinary analyses in toxemia.

Today the main points at issue concern the scope of the toxic form of hyperemesis, the significance of the urinary changes connected with it, the relation between the toxic symptoms of early pregnancy and eclampsia in the late months, while opinions regarding the pathogenesis of eclampsia still remain uncertain.

Regarding the relation of toxic and other forms of vomiting it is clear that any cause of vomiting may be operative in pregnancy. Yet the characteristic hyperemesis of gestation is a very definite clinical entity, and I think the only safe position to take is that it is always of toxic origin, and that an anatomical basis of the disease is found in the parenchymatous degeneration of the liver and kidneys

<sup>23</sup> Toxemia of Pregnancy, *American Gynecology*, 1903, iii, 518; *New York Med. Jour.*, 1905, lxxviii, 295.

<sup>24</sup> The Path. Anat. and Pathogen. of the Toxemia of Pregnancy, *Amer. Jour. Obstet.*, 1905, li, 145.

<sup>25</sup> The Clinical Significance of the Urinary Nitrogen, *AMER. JOUR. MED. SCI.*, 1906, cxxxii, 751.

<sup>26</sup> The Metabolism in the Toxemia of Pregnancy, *Amer. Jour. Obstet.*, 1907, iv, 289.

<sup>27</sup> Pernicious Vomiting of Pregnancy, *Johns Hopkins Hospital Bull.*, 1906, xvii, 71.

<sup>28</sup> *New York Medical Journal*, 1906, lxxxiii, 897, 957.

which there is abundant reason for believing is present in every such case. It is especially important to urge that the severe and persistent cases of the characteristic vomiting are always of autotoxic origin, notwithstanding the fact that they may cease after many apparently trivial procedures. Here I am reminded of the observation of Strauss,<sup>29</sup> who saw long-standing hyperemesis stop when the patient was anointed with holy water forty-eight hours before her death.

The available data indicate that the ordinary vomiting of pregnancy is the early sign of a continuous train of metabolic disturbances which end in fatal hyperemesis, malignant jaundice, and acute yellow atrophy. The pathogenesis of the early toxemia is a complex subject, but the evidence points to functional disturbance of the liver of metabolic origin as the essential factor. Tracing the origin of this metabolic disturbance, one is led directly to such factors as the hereditary predisposition, the previous condition of the patient, the cessation of the menses, the influence of the nervous system, the increased demands on metabolic activity, the sudden loss of an adequate food supply, and functional disturbance of the thyroid and parathyroid glands. There is something in gestation that seems to call for a readjustment of metabolic processes. We cannot exactly define the nature of this influence, but I think its character is suggested by the fact that some animals eat little or no protein food during gestation. From the moment of conception there seems often to be a distinct reduction in the capacity to digest and adapt alien proteins, suggesting that the tissues of the embryo are built up chiefly from the maternal tissues and that a nervous mechanism shuts off the ordinary supply of alien food proteins.

The failure of menstruation seems to be an important factor in some cases, as has been shown by Keiffer.<sup>30</sup> There is a toxemia of menstruation which may exactly resemble that of pregnancy, both clinically and in the chemistry of the urine. Intestinal putrefaction figures prominently in a considerable group of cases with high and variable indicanuria. With a liver defective in metabolic, detoxicating, and biliary functions, a rich protein diet is imperfectly digested and metabolized, indol and other putrefactive products are formed in excess and in turn damage the liver still further, so that a vicious circle of influences is established leading at times to some very severe forms of auto-intoxication. Here, as shown by Dirmoser,<sup>31</sup> milk diet and intestinal hygiene may bring prompt relief.

The element of starvation is of undoubted importance in some patients, and in prolonged cases must be charged with the extreme emaciation which occurs. Indeed, it has been claimed that starvation accounts for all the urinary changes in some cases and robs these

<sup>29</sup> Amer. Jour. Obstet., 1906, liii, 164.

<sup>30</sup> La menstruation dans ses rapports avec la pathologie gén., Jour. l'Obstétrique, Paris, 1897, ii, 289.

<sup>31</sup> Der Vomit Gravidarum, Wien, 1901.

urinary signs of any particular significance. As this has been the chief criticism raised against the present interpretation of hyperemesis, it seems desirable to consider it in some detail.

It may first be conceded that in some cases of hyperemesis the urinary changes are wholly or chiefly the result of starvation suddenly established in an organism requiring production of energy from an unusual source. It is then necessary to point out that starvation is itself a definite and sometimes rapidly fatal toxic process. Fasting dogs not infrequently pass into a condition of acute intoxication with increase of nitrogen output, gastro-enteritis, degeneration of the liver, and death (Schulz).<sup>32</sup> From the extensive literature on starvation one may refer to the recent study of Bianchi,<sup>33</sup> who finds that fasting mice and rabbits present granular degeneration of the liver and kidneys similar to that occurring in aseptic autolysis or produced by infusion of hypotonic salt solution. This condition he designates as *tonolysis*. In the later stages the fat and glycogen of the liver disappear, nuclear pyknosis and karyorrhexis and cell necrosis occur, and this condition he calls *toxolysis*. From simple tonolytic changes the animals may recover, but the toxolytic condition is self-perpetuating and the animals die in spite of food. In view of these observations, which are in line with many studies of similar import, it must be said that if starvation accounts for the toxemia of pregnancy, the condition still belongs among auto-intoxications, while the importance of the urinary signs of starvation becomes increased rather than diminished.

But neither the clinical symptoms nor the pathological anatomy nor the urinary chemistry of this toxemia are those of pure starvation as it occurs in other subjects. Starvation is not marked by persistent vomiting, pruritus, salivation, jaundice, maniacal delirium, and a fatal course in ten days or two weeks. The organs in fatal starvation do not show extensive grades of fatty degeneration with necrosis of large portions of the liver lobules or advanced hepatic atrophy. They show simple atrophy of liver cords, granular degeneration, and focal necroses. Regarding the significance of the urinary changes in toxemia, it is difficult to determine how far they should be referred to the simple withdrawal of food or to what extent they signify an injury to important organs. In some cases the total nitrogen is low, the urea low, ammonia high, rest nitrogen low, and acetone bodies are present. Such changes may seem to result from simple inanition, and to have no further significance, yet the validity of this view is by no means certain. In professional fasters a high ammonia ratio means the consumption of tissue proteins and fats in the absence of carbohydrates, but not that the organism is incapable of maintaining normal metabolism. In toxemia a similar ammonia

<sup>32</sup> Arch. f. d. gesam. Physiol., 1899, lxxvi, 379.

<sup>33</sup> Leber- und Nierenzellen während d. Verhungerung, Frankfurter Ztschr. f. Path., 1909, iii, 723.

ratio means that the patient is incapable of digesting, absorbing, and probably of burning the supply of proteins, fats, and carbohydrates that is usually forced upon it. The urinary signs of the two conditions may be similar, but the clinical significance of these signs is entirely different.

In other cases the total nitrogen is high, 10 to 12 grams, without strict relation to the nitrogen intake, the urea and ammonia are low, but the rest nitrogen is increased 200 to 300 per cent. I know of no similar urinary findings in starvation in other subjects. They may occur, possibly in the cyclic vomiting of children, but if so they must belong to Bianchi's toxolytic stage of the process of starvation, in which there are serious lesions of the liver. Such conditions, however, are common in the toxemia of pregnancy, especially when jaundice points to disturbance of the liver. Many patients seem unable to appropriate the available food supply, and show their worst symptoms shortly after a full meal. These attacks are not due to starvation in any proper use of the word, but in all probability they result from failure to metabolize the products of digestion. Here the theory of defective desamidization seems to apply, as the rest nitrogen of these patients is usually high.

Some years ago Scholten,<sup>31</sup> by administering glucose, greatly reduced the high ammonia of the urine in hyperemesis without affecting the other symptoms. Wolf and I confirmed this observation for certain moderately severe cases, and drew the conclusion that hyperemesis is not an acid intoxication.

Underhill and Rand<sup>35</sup> have recently reported an experiment of this sort in a severe case receiving 75 to 300 grams of dextrose by rectum. During the first five days the ammonia rose in spite of the dextrose. It began to fall when the dextrose was reduced from 300 to 75 grams. The reduction from 2.46 to 0.67 gram (41 to 20 per cent.) from the fourth to the ninth day failed to bring the ammonia as low as it was before the dextrose was begun, and part of this fall must be referred to the reduction in total nitrogen from 6 to 3.24 grams. From the ninth day the ammonia rose steadily in spite of dextrose, reached a higher point than before (2.04 grams, 57 per cent.), and the pregnancy had to be terminated. On the day of the lowest ammonia the patient was not making as much urea as on the day of highest ammonia, while the symptoms were not relieved. The urea formation was therefore a better index of the patient's condition than was the ammonia under dextrose therapy. If this experiment shows anything more than unexplained variations in ammonia excretion, it demonstrates the impossibility of controlling the ammonia and the symptoms with dextrose. While the dextrose seemed to have a temporary influence in correcting the acidosis, its chief

<sup>31</sup> Beiträge z. Geb. u. Gyn. (Hegar), 1900, iii, 3.

<sup>35</sup> The Peculiarities of Nitrogenous Metabolism in Pernicious Vomiting of Pregnancy, Arch. Int. Med., 1910, v, 61.



influence was to transfer the source of energy from protein to carbohydrate, thus reducing the total nitrogen and obscuring the deficiency in urea-forming function. I interpret the experiment as showing chiefly that both the urea-forming and the glycogenic functions were deficient.

The experiments with glucose do not, therefore, rob the urinary analysis of its value as a diagnostic sign, since ammonia is a measure of a toxic form of starvation and at the same time of the urea-forming function. In spite of its antiketogenic power glucose does not greatly or permanently reduce the ammonia, and, although a nutrient, it does not relieve the symptoms. Three hundred grams of glucose ought not only to correct the acidosis, but it should relieve the symptoms of simple hunger, but its effects in hyperemesis show that this condition is something more than lack of food. Thyroid extract, which is not a nutrient, not only corrects the acidosis of toxemia, but it relieves the symptoms, probably because it improves nitrogenous metabolism and facilitates urea formation.

The high rest nitrogen of many cases of toxemia we found to be a very significant feature of the urinary changes. This increase, which is partly of amino-acids, may be missing in some cases in which the ammonia runs high, but in others it may be very pronounced, and being often the only notable urinary change, we are disposed to think that defective desamidization is an important factor in some phases of the disease. Leathes<sup>36</sup> recognizes the importance of this high undetermined nitrogen, but Underhill would discard entirely the theory of defective desamidization, and asserts that there is no evidence that it existed in our reported cases. Yet in support of this statement he refers only to a class of cases which were grouped together partly because they showed chiefly high ammonia and little or no sign of defective desamidization, but he ignores a larger group in which the rest nitrogen was high.

The clinical significance of the rest nitrogen has been doubted also on the ground that this fraction in many cases in which it is high is yet not above the limits observed by Folin<sup>37</sup> in certain apparently normal subjects. The total rest nitrogen recorded by Folin for normal subjects was usually distinctly below 1 grain, but in a very few cases for short periods it rose to 1 gram and once to 1.34 grams. Underhill assumes that such differences in the rest nitrogen of apparently healthy individuals are "merely indications of the variation which may occur in normal metabolism." Yet the validity of this assumption may be questioned. Wolf and I have examined the urine of many normal subjects, and have found, as a very general rule, that when the rest nitrogen in adult men on mixed diet rises above 1 gram, or 10 to 15 per cent., the subjects are liable to attacks of indigestion, constipation, headache, migraine,

<sup>36</sup> Acidosis in Pregnancy, *Proc. Royal Society*, 1908, i, No. 5, Path. Sec., p. 131.

<sup>37</sup> Analyses of Thirty Normal Urines, *Amer. Jour. Physiol.*, 1905, xiii, 45

nervous irritability, urticaria, and pruritus or other skin affections. Johnston and Schwartz<sup>38</sup> have found a close relation between the rest nitrogen and the course of certain skin diseases. In all these cases the high rest nitrogen must be taken as a sign of defective metabolism, and not as an unimportant peculiarity of normal metabolism without clinical significance. I think, therefore, that one must not compare the rest nitrogen in toxemic women with that of "healthy" men on a starch-cream diet, but only with that of the subject herself when free from toxic symptoms. The rest nitrogen dropped from a comparatively high to a relatively low figure in so many of our cases when they became free from symptoms that we are disposed to maintain the opinion that this high rest nitrogen was in some way connected with the production of these symptoms..

Another source of doubt as to the dependence of urinary changes upon functional disturbance of the liver has been assumed to exist in the results of certain experimental lesions of this organ. Pearce and Jackson<sup>39</sup> destroyed considerable portions of the liver by injections of hemolytic serum, but found little coincident change in the urinary nitrogen. It seems doubtful if these experiments have any direct bearing on the significance of the urinary changes in toxemia of pregnancy. The hepatic lesions of toxemia are the result and not the first cause of the impairment of function. They must arise from secondary disturbance in the nutrition of the organ cells, and do not exist until that disturbance has reached a certain intensity. When one injects hemolytic serum into a healthy animal much of the liver may be destroyed, but the remaining portions preserve their functions and the metabolism is only slightly affected. When, however, the limit of safety has been passed by such procedures as the injection of acid into the bile ducts, or by the establishment of an Eck fistula, symptoms and urinary changes develop rapidly and with great violence, as in eclampsia.

Pearce and Jackson call attention to the fact that in two of their animals in which the liver showed diffuse degeneration as well as focal lesions the nitrogen partition was distinctly altered.

The dependence of urinary changes upon lesions of the liver was firmly established by Minkowski,<sup>40</sup> Nencki and Pawlow,<sup>41</sup> and Salaskin and Zaleski,<sup>42</sup> and it seems unlikely that this fundamental principle of experimental pathology will ever be discredited.

An obscure feature of the urinary chemistry in toxemia is the occurrence of a nearly normal nitrogen partition in the late stages of prolonged and fatal cases. I can offer no satisfactory explanation for such results. They remind one of cases of diabetes in which sugar and acidosis disappear shortly before death. It seems possible

<sup>38</sup> New York Med. Jour., 1909, lxxxix, 535, 590, 636.

<sup>39</sup> Experimental Liver Necrosis, Jour. Exper. Med., 1907, ix, 552.

<sup>40</sup> Arch. f. exper. Path. u. Pharm., 1886, xxi, 41.

<sup>42</sup> Ztschr. f. phys. Chemie., 1900, xxix, 517; 1902, xxxv, 246.

<sup>41</sup> Ibid., 1893, xxxii, 161.

that the metabolism becomes reestablished on a low and insufficient scale, while the patient dies from secondary degenerative processes established in the organs.

In view of these and many other uncertainties surrounding the interpretation of urinary analyses, I can only repeat that great caution is needed in basing clinical procedures on the results of these analyses. Their chief value is found as a basis for preventive measures. Our experience during the last three years has fully justified the expectations of their clinical value. They are a means of separating the safe from the hazardous pregnancy. They have repeatedly given warning of an unsafe condition and led to the use of dietetic and hygienic measures which have improved the metabolism. I have known their warning to have been persistently neglected with patients who eventually lost their lives, and whose physicians are now converts to the method.

While the practical value of the study of the nitrogen partition in these cases seems assured, the exact significance of some of the urinary changes must be sought in future investigations. Complete urinary analyses in a large number of normal pregnancies with various diets are much needed as a standard of comparison. Extended analyses of all the nitrogenous substances over long periods in toxemic cases, with careful estimation of the diet, would doubtless throw much light on the uncertain points now under discussion. The metabolism of fats, carbohydrates, and inorganic substances, as well as of the nitrogen, deserves attention. As has been urged by Leathes, it is especially the composition of the "rest nitrogen" that demands investigation, and recently there have been important contributions to our knowledge in this difficult field. Although amino-acids make a considerable part of this fraction, the peptones of the older observers, Salkowski's colloidal nitrogen precipitable by alcohol, and Savarè's<sup>43</sup> non-dialyzable nitrogen, all belong more or less in this category. Marriott and Wolf<sup>44</sup> have shown that Salkowski's colloidal nitrogen, while much increased in toxemia, does not correspond to the amino-acid fraction. Ginsberg<sup>45</sup> finds that the rest nitrogen is chiefly composed of oxyproteic and other amino-acids, and that the nitrogen referable to wholly unknown substances in human and dog urines is not large. This conclusion, as well as Savarè's studies, seem to strengthen the basis of the theory of defective desamidization, since a deficiency of this process would tend to increase the oxyproteic acids and other non-dialyzable protein cleavage products in the urine. Yet we are not committed to this theory as a complete explanation of toxemia, but only as a partial explanation. Its influence is most apparent in subjects taking some protein food,

<sup>43</sup> Der Gehalt der Frauenharns an adialyablen Stoffen, *Beitr. z. chem. Physiol.*, 1907, ix, 401.

<sup>44</sup> Colloidal Nitrogen in the Urine, *AMER. JOUR. MED. SCI.*, 1907, cxxxiii, 404.

<sup>45</sup> Ueber d. Oxyproteinsäurefraction des Harns, *Hoffmeister's Beitr.*, 1907, x, 410.

while in cases that are retaining no food and burning only body proteins its importance is less apparent.

Regarding the close relation of acute fatal hyperemesis and acute yellow atrophy the evidence seems to me conclusive. Clinically hyperemesis pursues an acute or fulminant, a subacute, or a chronic course. In the fulminant cases one finds the liver often small, of greatly reduced consistence, with extensive fatty degeneration, and central or zonal necrosis. There must be some additional factor to account for the widespread complete destruction of liver tissue seen in many cases of acute yellow atrophy, and this factor may possibly be found in the solvent action of extravasated bile. There are also indications that closer clinical observation and chemical study may reveal some specific form of intestinal putrefaction leading to polycholia, as the distinguishing element separating acute yellow atrophy from the cases not marked by jaundice. With the exception of jaundice and complete destruction of liver tissue hyperemesis and acute yellow atrophy arise under similar conditions in pregnancy, pursue much the same course, and intermediate cases between the typical forms, both clinical and anatomical, are occasionally observed.

While 60 per cent. of the cases of hyperemesis, it is said, recover, there are certain sequels which are attached to the condition. It would appear doubtful if the patient ever fully recovers during gestation, and premature ageing of the child-bearing woman may in large part be due to repeated auto-intoxication during pregnancy. Toxemia is also a fruitful source of foetal death, and the foetal organs show the same changes as the maternal. Obstetrics does not yet charge itself with responsibility for the condition of the viable foetus at birth, but while there are remarkable exceptions, the infants of toxemic mothers are often imperfectly developed, sometimes show definite constitutional defects, and are especially liable to the disorders of infancy.

In the maternal organism the most important sequel of toxemia in the early months is nephritis in the later periods. That nephritis is a frequent result of the early toxemia, I am convinced is a fact from having observed several striking cases which appeared to have recovered from persistent vomiting in the early months but later developed active nephritis. In cases of eclampsia, in which nephritis is nearly constant, a history of previous toxemia can nearly always be established. In a third group of cases toxemia continues up to the outbreak of eclampsia. Although it is impossible to define the exact nature of this connection, there are a number of observations which show that several of the factors concerned in hepatic toxemia act as nephrotoxic agents. There is considerable evidence to show that the acidosis of early toxemia may contribute to the albuminuria of later months. In dogs whose livers had been injured by potassium

cyanide or chloroform Richards and Howland<sup>46</sup> found that small doses of indol caused severe damage to the kidney. In hepatic toxemia with intestinal putrefaction similar conditions exist, favoring unusual toxic effects on the kidney from indol and other intestinal poisons. Studying the metabolism of typhoid-fever convalescents, Wolf and I<sup>47</sup> found that early ingestion of meat may be followed by excessive indicanuria, excretion of unchanged amino-acids of the food, and albuminuria, constituting the so-called "febris carnis." There is here an obvious parallel with the excessive meat diet which many women indulge in after the first relief from the early vomiting of pregnancy. While none or all of these factors may fully explain the relation between nephritis and toxemia, they may render more acceptable the view that such a relation exists. St. Blaise has already discussed this subject at length.

The late nephritis of pregnancy, whatever its origin, becomes of great importance in its relation to eclampsia. The problem of the pathogenesis of this disease still seems far from complete solution.

The transfer of interest from the kidney to the liver as the organ chiefly responsible, the search, led by Weichardt,<sup>48</sup> for a specific poison in the placenta or syncytium, the inculpation of the foetus as the source of the poison, and the numerous expedients employed to reproduce the disease are familiar phases of the history of research in this field. Among the most systematic efforts yet made to reach a solution of the problem, that of Dienst<sup>49</sup> deserves particular notice. He first reaches the important conclusion, which would seem to be final, that eclampsia is not caused by a poison emanating from the foetus, for he found that the fibrin and leukocytes are lower in the foetus and the thrombotic lesions appear later than in the mother. Against this view stands also the occurrence of eclampsia in cases of molar pregnancy, (Hitschman,<sup>50</sup> Kroemer,<sup>51</sup> Dienst). The placental theory he also abandons, since all previous efforts to find specific changes in the eclamptic placenta had failed and he himself had found entirely normal placentas in eclampsia. Dienst then commits himself to the theory that the thrombotic lesions and the chief symptoms of eclampsia are caused by the sudden destruction of excessive numbers of leukocytes, which he believes gather in the distended veins of the uterus and placenta and during labor discharge excess of fibrin ferment into the circulation. Several difficulties stand in the way of this hypothesis, among which are the absence of any definite cause of such destruction of leukocytes; the predominance of thrombi in the liver over those in the lungs; the occasional absence of thrombi;

<sup>46</sup> Archives of Pediatrics, 1907, xxiv, 401.

<sup>47</sup> The Nitrogenous Metabolism of Typhoid Fever, Archives Int. Med., 1909, iv, 330.

<sup>48</sup> Exper. Studien u. d. Eclampsie, Deutsche med. Woch., 1902, 224. Ueber Erweissub-erempfindlichkeit, Centr. f. Bact., 1909, lii, 77.

<sup>49</sup> Pathogenese d. Eclampsie, Arch. f. Gyn., 1908, lxxxvi, 314.

<sup>50</sup> Eclampsie in fünf Schwangerschaftsmonate, ohne Fetus, bei Blasenmole, Centr. f. Gyn., 1904, 1089.

<sup>51</sup> Cited by Dienst.

the occurrence of leukocytosis after, but not before, the convulsions; and the absence of excessive fibrin deposits in the placenta. Moreover, fibrin ferment cannot account for the high blood pressure and the nephritis, two of the conditions generally regarded as most significant.

It is interesting to note that Dienst accepts the near relation or possible identity of pernicious vomiting and eclampsia and states that acute yellow atrophy must be due to the same factors as eclampsia, since convulsions are not always present in the latter condition. Eclampsia, he thinks, occurs only when the liver and kidneys are incompetent.

Hofbauer's view that an eclamptic toxin arises from the placenta is probably shared by the majority of observers. In the modified forms of a specific syncytiotoxin, now extended to include the element of anaphylaxis, it is maintained by Weichardt and others. The chief evidence in its favor is the clinical experience that the best treatment of eclampsia is immediate delivery of the placenta, and yet eclampsia occurs after delivery and in molar pregnancy.

I was at one time much impressed by the theory of a placental toxin, but have been unable to secure any definite evidence in its favor. In the histological study of a series of eclamptic placentas I found, as had others, no specific changes and sometimes no changes whatever. One's attention may be attracted by the presence of many placental blood clots in various stages of disintegration, and the suggestion arises that a hemolytic and blood-coagulating agent from such old clots may account for the hemolysis and thromboses of the disease. But I have found eclamptic placentas wholly free from such clots, and have been unable to find evidences of hemolysis in every case of eclampsia, and I do not think that a hemolytic and blood coagulating agent from the placenta will explain the lesions of the disease. Pearce concludes from a study of the action of hemolytic agents that the severe lesions of the liver produced by them are not those of eclampsia.

There have been many attempts to produce the lesions and symptoms of eclampsia by means of salt solution extracts of the placenta. These experiments usually result in extensive thromboses variously distributed according to the mode of introduction, but neither the lesions nor the symptoms exhibit the finer qualities of eclampsia, and the experimenters seem to have overlooked the fact that salt solution extracts of almost any normal organ contain nucleoproteids in a form in which they are active blood coagulants. Considering the possibility that antolytic products of the placenta might be concerned in the thrombotic lesions, Dryfuss,<sup>52</sup> in the Cornell Laboratory, compared the chemical composition of eclamptic placentas with normal and antolyzed normal placentas. He succeeded in showing

<sup>52</sup> Chem. Untersuch. u. d. Aetiologie d. Eclampsia, *Biochemisches Zeitschr.*, 1908, vii, 493.  
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that the eclamptic placenta on delivery has suffered autolytic changes, as do the other organs of the body, but not that it possesses any specific toxic action. Mohr and Freund<sup>53</sup> believe they have found the active toxic agent of eclampsia in oleic acid, which they isolated in comparatively small amounts from the placenta, but Polano<sup>54</sup> discards this theory on the ground that oleic acid is not found in increased or sufficient quantities either in the placenta or in the blood. In view of these indecisive results in so many directions, I am inclined to think that a specific eclamptic toxin does not exist in the placenta, and that the therapeutic results of its early expulsion from the uterus must be explained in some other way.

Various attempts have been made to demonstrate in the blood serum a specific toxic substance in eclampsia. Chambrelent,<sup>55</sup> and Ludwig and Savor<sup>56</sup> found that rabbits succumbed to intravenous injections of either normal or eclamptic serum, but the latter was distinctly more toxic. Yet Volhard<sup>57</sup> and Schumacher<sup>58</sup> both failed to find any difference in the action of the two classes of serum. In 1906 Semb<sup>59</sup> tested the toxicity of eclamptic serum in rabbits previously immunized against normal serum. He hoped in this way to eliminate the toxic effects of the normal serum. Of twenty animals, ten (50 per cent.) died during the immunization against normal serum, and of the remaining ten, five (50 per cent.) died from the further injections of eclamptic serum. In the immunized animals the eclamptic serum, in doses of 4 to 6 c.c. per kilo, sometimes produced symptoms and lesions closely resembling some of those of eclampsia, but some animals were entirely refractory and showed neither lesions nor symptoms. The intraperitoneal injection of 40 c.c. of eclamptic serum proved harmless. Semb was not fully convinced by these results that he had demonstrated in the serum of eclampsia a definite toxic agent, for exactly the opposite conclusion seems to be equally justified. What Semb really accomplished appears to have been that he immunized the rabbit's red cells against the hemolytic action of human serum, but at the same time developed strong precipitins against human blood proteins, the action of which was instrumental in producing the lesions. It should be noted also that animals do not develop a true immunity against alien organ proteins, but may become increasingly susceptible to their action.

Proceeding from an entirely different point of view, Zweifel<sup>60</sup> concluded that lactic acid is the main toxic agent in eclampsia, and he succeeded in isolating definite quantities of this acid from the blood, but it is now generally conceded that lactic acid is one of the products

<sup>53</sup> *Exper. Beitr. z. Pathogen. d. Eclampsie*, Berl. klin. Woch., 1908, 1793.

<sup>54</sup> *Oelsaurewirkung als Ursache d. Eclampsie*, Zeit. f. Geb. u. Gyn., 1909, lxx, 581.

<sup>55</sup> *Gazette méd. de Paris*, 1894, 9th ser., i, 365, 371.

<sup>56</sup> *Monatschr. f. Geb. u. Gyn.*, 1895, i, 447.

<sup>57</sup> *Ibid.*, 1897, v, 411.

<sup>58</sup> *Beiträge z. Geb. u. Gyn.*, 1901, v, 257.

<sup>59</sup> *Exper. Untersuch. z. Pathogenese d. Eclampsie*, Arch. f. Gyn., 1906, lxxvii, 63.

<sup>60</sup> *Zur Aufklärung der Eclampsie*, Arch. f. Gyn., 1904, lxxii, 1; lxxvi, 536.

of the deranged metabolism of the disease, results chiefly from the convulsions, and is not the cause of these convulsions.

Thus, all efforts to discover a specific poison of eclampsia in the foetus, in the placenta, or in the blood have failed, and some other conception of the disease would seem to be necessary.

It appears not improbable that some diffusible toxic agent may be closely connected with the symptoms of eclampsia, but the general facts of the disease strongly indicate that the eclamptic seizure can arise only in an organism long prepared for it by disturbance of metabolism and the associated organic changes. The great majority, or possibly all eclamptic seizures are preceded by a period, sometimes called the preëclamptic state, marked by elevated blood pressure, headaches, oedema, and intolerance of protein food. These are the symptoms of a nephritis, and the kidneys in fatal cases almost invariably show that a nephritis, usually of the glomerular type, has existed for some time. The urine at this time commonly shows reduction in quantity, low urea, and high rest nitrogen. These features persist throughout the eclamptic seizure, and indicate, as in the other forms of toxemia, defective urea-forming function of the liver and defective desamidization. If there is any single distinguishing causative element in eclampsia, I believe it is to be found in the nephritis and not in specific poisons from foetus, placenta, or uterus.

The exact mode of origin of the eclamptic seizure still remains the obscure problem, but that it develops through an abrupt disturbance of metabolic functions is a view toward which attention is now generally directed. Zweifel has done much toward establishing this hypothesis, by showing the immense reduction in the so-called oxidative functions of the body, as indicated in the high ammonia and unoxidized sulphur of the urine. Wolf and I drew the same conclusion from the study of the nitrogen partition, but we believe that the metabolic disturbance is not merely defective oxidation, but is more complex, as is indicated by the high rest nitrogen. Savarè has found that the non-dialyzable fraction of eclamptic urine is ten to twenty times that of normal urine, but he has not reported on the chemical nature of the substances concerned. The metabolic disturbance appears to have the same general characters as in other forms of the toxemia of pregnancy, but it acts more rapidly and in an organism suffering from nephritis.

During the eclamptic seizure three definite effects are produced: (1) A remarkable rise in the blood pressure; (2) a pronounced injury to the nervous system; (3) coagulation of the excessive fibrinogen of the blood. That these effects are due to certain agents arising in the course of disturbed metabolism there can be little doubt. In some predisposed subjects the eclamptic seizure arises shortly after the ingestion of a full meal rich in meat. Here one looks naturally among the products of protein digestion for the toxic agent. Ammonia, amino-acids, and xanthin may be incriminated, for these are



incompletely metabolized by the injured liver and imperfectly eliminated by the kidneys. I have been much impressed by the rapid rise in the urinary ammonia during the eclamptic seizure and its rapid fall as the patient improved. This rise in the ammonia may be overlooked unless one examines the urine at three or six hour intervals. It seems to be unaccompanied by corresponding rise in the acetone bodies. It is possible that acute ammonia poisoning may be concerned in the symptoms of such cases. Ammonia is highly diffusible, raises blood pressure, is a violent nerve poison, and its effects pass off rapidly. So far as I know it does not facilitate blood coagulation, but it causes severe degeneration of organ cells and probably of leukocytes. Some years ago the Russian observers, Nencki and Pawlow, and Salaskin and Zaleski concluded that poisoning by ammonium carbamate is chiefly responsible for the symptoms following extirpation of the liver or the Eck fistula. There have been a few criticisms of this opinion, but no definite refutation of its experimental basis. Ammonia poisoning is perhaps incapable of explaining all the symptoms of eclampsia, but that it figures in the convulsions is an hypothesis which I believe is worthy of consideration.

Recent studies of the physiology of the thyroid and parathyroid glands suggest that primary disturbance of the functions of these organs may be concerned in the toxemia of pregnancy. After parathyroidectomy there is an increase in the ammonia content of the blood. The convulsions following parathyroidectomy MacCallum and Voegtlin<sup>61</sup> attribute to loss of calcium, but Berkley and Beebe<sup>62</sup> offer considerable evidence to show that these convulsions are due to some metabolic poison, possibly ammonia or xanthin, and that the calcium loss is a secondary effect associated with starvation.

It has been clearly shown that after extirpation of the thyroid and parathyroid, or of parathyroid alone, the toxic symptoms may be greatly intensified by a meat diet and reduced by milk diet. There is here a striking parallel with the toxemia of pregnancy. The meat diet offers abundant sources of ammonia, amino-acids, and xanthin. Carlson and Jacobson<sup>63</sup> find that in thyroid-parathyroidectomized animals the ammonia-destroying power of the liver is reduced 26 to 30 per cent., and they conclude that the increase of the ammonia of the blood is due in part to depression of the liver rather than to acidosis. In the case of certain animals in which there are no symptoms there is no increase in the ammonia of the blood and no depression of the ammonia conversion power of the liver. It is interesting to note that in these animals there is extreme salivation.

<sup>61</sup> On the Relation of the Parathyroid to Calcium Metabolism, Johns Hopkins Hosp. Bull. 1908, xix, 91.

<sup>62</sup> A Contribution to the Physiol. and Chem. of the Parathyroid, Jour. Med. Research, 1909, xx, 149.

<sup>63</sup> Proc. Soc. Exper. Med. and Biol., 1909, vol. 1.

The experimental studies in this field therefore have furnished important evidence inculcating the thyroid and parathyroid in the pathogenesis of the toxemia of pregnancy, favoring the view that the disorders are of metabolic origin, and that the high urinary ammonia in toxemia may result from deficiency of hepatic function rather than from simple starvation. They may also explain the remarkable therapeutic effects of thyroid extract, on which Foulkrod<sup>64</sup> and Ward<sup>65</sup> have reported, and which have been observed in a considerable series of cases soon to be reported by Beebe.

I have examined the thyroids and parathyroids in several fatal cases of toxemia, but have found no significant changes except in one case (No. 30) reported in 1907. Here one parathyroid was swollen to several times its normal dimensions and the cells were of very large size. I have found great variations in the histology of the thyroid in toxemia, but no constant changes. In some cases the gland appeared to be overacting, in others it was undersized and relatively inactive.

That pernicious vomiting, acute yellow atrophy, and eclampsia are somewhat different clinical manifestations of essentially the same disorder of metabolism is a view I ventured to state in 1904, and further evidence in its favor was offered in 1907. The evidence supporting this belief consisted in the incidence of all three disorders chiefly or exclusively in gestation, the occurrence of cases intermediate between pernicious vomiting and yellow atrophy and between yellow atrophy and eclampsia, and the frequent development of eclampsia in patients who had previously suffered from hyperemesis. Chemical studies seemed to give further evidence of the general identity of the disorders, pointing to the hepatic origin of hyperemesis and yellow atrophy and the combined hepatic and renal origin of eclampsia. Williams, however, has rejected the hypothesis of a close relation between eclampsia and the other forms of toxemia, although recognizing the connection between hyperemesis and acute yellow atrophy. He based his dissent on the absence of ammonia excess in the urine of eclampsia and on the striking differences in the lesions of hemorrhagic hepatitis from those of the other forms of toxemia. Yet the occurrence of high ammonia ratios in eclampsia has been amply proved by Zweifel, and the possibility of overlooking the rise in ammonia has already been mentioned.

Time forbids a full discussion of the significance of the hepatic lesions, but I may mention some of the features of the pathological anatomy of toxemia which warn against separating eclampsia on account of its peculiar hepatitis. The typical eclamptic liver is found chiefly in rapidly fatal cases. If the disease is prolonged, the convulsions not prominent, or if jaundice be present, one is apt

AMER. JOUR. MED. SCI., 1908, cxxxvi, 541.  
<sup>65</sup> Surgery, Gynecology, and Obstetrics, 1909, vii, 617.

to find the hepatic lesion indistinguishable from that seen in some cases, which on account of the absence of convulsions are called acute yellow atrophy. On the other hand convulsions occur in some cases in which the hepatic lesion is typical of acute yellow atrophy. This intermingling of lesions and symptoms was long ago described by Virchow,<sup>66</sup> v. Frerichs, Klebs,<sup>67</sup> and Stumpf, and was early noted in my own experience in this field. When one inquires into the mode of origin of the capillary thromboses of the liver, one finds that an autolysis of the liver with injury of the endothelial cells is probably an essential underlying condition. This interpretation has been fully worked out by Konstantinowitsch,<sup>68</sup> has been stated in reports of my own cases, and is accepted by Hofbauer. I believe, therefore, that an acute degeneration of the liver arising in the course of acute disturbance of its metabolic functions is the essential part of the hepatic changes in eclampsia, and that the capillary thromboses are more secondary results of the action of a blood-coagulating agent in the liver and other organs. Dienst now accepts the view that eclampsia and acute yellow atrophy are due to the same general causes, the chief of which is the failure of the metabolic functions of the liver. Hofbauer expresses the same opinion.

Notwithstanding the obscurities that still exist, it must be admitted that the past decade has witnessed important progress in our knowledge of the peculiar auto-intoxications of pregnancy. The earlier studies in pathological anatomy have been reviewed, extended, and systematized, and the interpretation of lesions has been rendered more significant. The recognition of clinical symptoms, especially their wide diversity, has been facilitated, and the true import of early signs has been much more widely accepted. The dangers of chloroform poisoning and its influence in the severe hepatic lesions of many cases has been sufficiently impressed to be generally heeded. In systematic urinary analyses we have a means of recognizing the character and gravity of the metabolic disorder, as well as a basis for instituting hygienic and dietetic measures with a view of forestalling and preventing the dangerous stages of the disease. Urinary analyses may not tell when to empty the uterus, but they may suggest treatment that will make it unnecessary to empty it at all. Finally, the indications for treatment have been more clearly defined. Doubtless there are necessarily fatal forms and stages of all types of toxemia, but with the great majority of patients the relief of acidosis, the hygiene of the intestine and correction of indicanuria, the careful control of the diet, with reduction or exclusion of proteins, and the intelligent use of thyroid extract, should control the milder cases and greatly reduce the mortality in the severe forms of the disease.

<sup>66</sup> *Contrib. f. allg. Path.*, 1891, ii, 805.

<sup>67</sup> *Ziegler's Beitr.* 1888, iii 1.

<sup>68</sup> Konstantinowitsch, *Beitr. z. Kennt. d. Leberveränderungen bei Eclampsie*, *Beitr. z. path. Anat.* (Ziegler), 1907, xl, 483.

## CHRONIC FAMILY JAUNDICE.

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IN recent years considerable attention has been attracted to a remarkable disease, characterized by chronic non-obstructive jaundice with enlargement of the spleen, and usually occurring in hereditary form, or in several members of one family. In spite of a goodly number of reports from Germany, England, and especially from France, the condition has attracted little notice in this country, and no articles on the subject have appeared. That chronic family jaundice is far from rare is shown by the fact that we have been able, within a short space of time, to investigate four such families.

The first accurate account of the disease was given by Minkowski in 1900, though Murchison, fifteen years before, described a family showing hereditary jaundice, and Hayem, in 1898, reported, under the title, chronic infectious splenomegalic icterus, cases which have since been shown to belong to the condition in question. The family reported by Wilson in 1890 also belongs here, but was not thoroughly investigated.

The important features are as follows: Jaundice appears in several members of a family, frequently in two, three, or even four generations. It dates either from birth, or is first noticed during adolescence, and persists throughout life, yet in spite of the long duration, the patient experiences little inconvenience from his complaint, and may attain an advanced age. The growth of these children is not interfered with. The icterus is usually not intense, there are no signs of obstruction of the bile ducts, and symptoms of cholemia, such as itching, slow pulse, xanthomas, and multiple hemorrhages, are lacking. The stools are highly colored, and the urine contains urobilin, but no bile. Enlargement of the spleen, which may reach huge proportions, is almost a constant feature, while the liver is usually not at all, or only slightly enlarged. As a rule, there is a moderate grade of anemia. "Bilious attacks" are extremely common, especially in youth; after an indiscretion in diet, a period of constipation, or without obvious cause, the patient feels tired and depressed, the jaundice deepens, and there is repeated vomiting of bile. Headache, diarrhoea, and slight fever are occasionally noted. After a day or two the attack passes off, to recur usually several times a year. Attacks of abdominal pain, located in

the epigastrium or right hypochondrium, are met with in a large proportion of cases, and are due, as will be shown later, to a complication with gallstones. The enlarged spleen often causes a feeling of weight and pressure in the left side of the abdomen, and pain in this region, sometimes accompanied by a friction rub, is a not infrequent occurrence, owing to a complication with perisplenitis. A history of nose-bleed, particularly during adolescence, is almost always to be obtained, but hemorrhages from other organs, and especially from the stomach and intestines, are not met with, an important distinction from splenic anemia and cirrhosis. Apart from the attacks mentioned above, the subjects, as Chauffard aptly remarks, are rather jaundiced than sick. However, there is often a feeling of lassitude and a tendency to somnolence.

**TYPES OF THE DISEASE.** Besides the usual form in which the disease is hereditary, and others in which it is familial, in the sense that several brothers or sisters are affected while the parents are not, there is a "congenital" form, in which the disease appears in only one of a family, and dates from birth. This latter type does not differ in any way from the common form, except in the absence of heredity. Another type is the so-called "acquired" form, in which the disease appears first in childhood or adolescence, rarely later. Many of the cases are undoubtedly identical with the hereditary form, in which it not seldom happens that the jaundice is first noticed in youth (such as our Cases V, VII, X, and XII). There is always a possibility that slight jaundice was present earlier, but escaped detection. In other cases the acquired form shows some divergences from the hereditary, especially in the severity of the anemia, which may even simulate pernicious anemia. In the cases of Stejskal and Chauffard the red count fell below one million, but pernicious anemia could be excluded by the morphology of the red cells, and the presence of *increased* fragility of the red cells; in pernicious anemia the fragility is *decreased*. The postmortem appearances in acquired cases have been identical with those in the hereditary type, and for the present it is permissible to conclude that the acquired and the hereditary form are only different manifestations of the same disease, just as we see in other diseases which are usually hereditary (such as progressive muscular dystrophy) cases which are apparently "acquired."

**THE JAUNDICE.** In well-marked instances the conjunctivæ are a lemon-yellow color, and the skin of the body is distinctly yellow, while the face is of a peculiar buff color which is quite characteristic. The greenish or blackish tint seen in long-standing total obstruction of the bile ducts is never present. In light cases the yellowness is apparent only on careful scrutiny. The jaundice varies in intensity from time to time, being more marked in some patients during the cold weather, in others in the summer. Fatigue and sometimes emotion may cause an increase in the jaundice, and at such times

the patients, as a rule, complain of lassitude and depression. Inter-current diseases, and even taking cold, may cause an increase. Once present, the jaundice persists throughout life. An apparent exception to this rule is seen in Plehn's first case, who was very yellow as a child, but never later, and at sixty-one showed only anemia and enlarged spleen. (No examination of the serum for bile was made.) Poynton and a few others have observed recurrent attacks of jaundice with only anemia and splenic tumor in the intervals. As the blood serum was not examined for bile, it may be questioned if a slight degree of icterus in the interval did not escape detection.

**THE URINE.** The urine is almost always high colored. Urobilin is present in the great majority of cases, being missed chiefly in those of slight intensity. Urobilinogen is also almost always to be found. On the other hand, bile is absent from the urine almost invariably, and when found is usually in small quantities and as a transitory phenomenon. The twenty-four hour amount is normal. There is frequently a deposit of urates, and sometimes of uric acid; in one of our cases (VII) showing such a deposit, the total endogenous uric acid was increased. We have found the normal urinary pigment (urochrome) constantly increased, and this accounts in large measure for the reddish-yellow color of the urine, which is present even in cases showing no urobilin. Hematoporphyrin is always absent.

**THE STOOLS.** In all reported cases the feces have been well-colored, and in those that we have examined they have seemed to contain an excess of pigment, judging from the intense orange or brown color. A marked reaction for urobilin is obtained with corrosive sublimate, and an intense fluorescence with Schlesinger's test for urobilin. These facts, together with the urobilinuria, point to an increased secretion of bile into the intestine, and Möller has, in fact, shown by quantitative methods that the total urobilin excretion in the urine and feces is considerably increased (400 milligrams in twenty-four hours). Unaltered bilirubin is absent or present only in traces. The guaiac test for occult blood has been uniformly negative in our cases. The feces show no excess of fat, starch, or muscle fibers, and quantitative analysis in one of our cases (VII) showed normal proportions of neutral fat, fatty acids, and soaps, as was to be expected. Constipation is often present, but not with regularity, several of our patients passing two or three soft stools daily.

**THE BLOOD.**—The serum always shows the presence of bile pigment, but not of urobilin. The important feature, which gives our chief clue to the nature of the disease, is the decreased resistance of the red cells to hemolyzing agents, or as it is sometimes called, the increased fragility. This was first discovered by Chauffard, and has been present, with very few exceptions, in all the cases in which it was looked for. The usual method of testing for it is by mixing the red blood cells, preferably after separation from the

plasma, with hypotonic solutions of sodium chloride of varying strengths, and noting the point at which hemolysis takes place. With normal blood hemolysis begins in salt solutions of 0.44 per cent., and is complete at 0.36 per cent. In the case of chronic family jaundice, however, hemolysis begins at 0.6 per cent., or even 0.7, and may be complete at 0.5 per cent. This marked decrease of resistance is all the more important, because in chronic obstructive jaundice the resistance is normal or *increased*. As Chauffard has shown, this lessened resistance is evident also when tested with other hemolytic agents, such as eel serum and antihuman serum. Hemolysins, however, have never been found in the blood serum, though often looked for, and hemagglutinins have been found in only one case (Hawkins and Dudgeon). Hemoglobin has been found in the blood serum in only two cases, those of Bettmann and Chauffard. Bettmann's patient frequently had attacks of prostration with increased jaundice after exposure to cold. The author was able to induce such an attack artificially by means of immersion of the hands in ice water, and then found large amounts of hemoglobin in the serum and later in the urine. In Chauffard's case oxyhemoglobin was found in the serum during a routine examination. Such phenomena are probably quite exceptional in chronic family jaundice, but are interesting in connection with the hemolytic theory of its causation. They do not prove any close relationship to paroxysmal hemoglobinemia.

A moderate anemia is the rule, with red counts usually in the neighborhood of three or four millions. The lowest count in the hereditary type was 1,500,000 (Benjamin and Sluka), while occasionally normal figures are reported, and in two cases abnormally high counts (Mosse, 7,800,000; Guinon, Rist, and Simon, 7,200,000). In Mosse's case, however, the jaundice was acquired at the late age of fifty-four years, so that it may be doubted if it belongs with the disease under consideration. It differed from the ordinary type of polycythemia by the lack of cyanosis and the presence of acholuric jaundice. In the other case, also acquired, the polyglobulia was transient and accompanied by cyanosis.

The color index is usually normal, the hemoglobin being reduced in proportion to the red count. The red cells are usually well colored. There is well-marked anisocytosis, with microcytes predominating. When measurements have been made, the average diameter has been found decreased. Thus out of six cases in which we measured the cells, the diameter was decreased in five, averaging 6.5 microns, and normal in one. Usually there is little poikilocytosis, and some polychromatophilia, but punctate basophilia is rare. Reticulation of the red cells, as brought out by the so-called "vital" method of staining, is apparently a constant feature, and is considered by Chauffard an important diagnostic sign if present in a considerable proportion of the cells. Nucleated red cells in

small numbers are often found, usually in the form of normoblasts. In two of our cases there were isolated megaloblasts, of the intermediate variety; that is, with small deeply staining nucleus. The blood plates are present in normal numbers. The leukocyte count is usually within normal limits, sometimes subnormal and exceptionally increased. The differential count shows nothing striking except for a tendency toward high values for the polynuclear neutrophils, and the occasional presence of rare myelocytes. The blood picture differs from that of the ordinary secondary anemia in the normal color index and the more frequent appearance of nucleated red cells.

**THE LIVER.** The liver is usually of normal size, or slightly enlarged, seldom reaching more than one finger's breadth below the edge of the ribs. Some have noted that during exacerbations of the jaundice the liver swells, to return to its former size after the attack is over. Signs of cirrhosis, such as hardness, irregularity, or marked alteration in size of the liver, ascites, and evidences of collateral circulation, are conspicuous by their absence. The bile, in the only case in which it was examined (our Case VII) was of a deep golden-red color, evidently very rich in pigment, and was sterile.

Attacks of abdominal pain resembling biliary colic have been observed in a large proportion of cases, and have been often supposed to be caused, in some mysterious way, by the disease itself. In two of our cases (VII and IX), however, gallstones were removed at operation, after which the attacks ceased, and in both our autopsies (Cases I and II) stones were found in the gall-bladder, so that we have no hesitation in declaring that these attacks are due to gallstones. A striking feature is the frequent onset of the colic at the time of puberty, a period at which ordinary cholelithiasis is seldom met with. The pain is sometimes located in the region of the spleen, and is then due to perisplenitis, for friction rubs have been heard over the spleen and inflammatory changes in the capsule have been found at autopsy. The pain of perisplenitis, however, is different from that of gallstone colic, being usually dull and not paroxysmal.

**THE SPLEEN.** The presence of splenic tumor forms one of the most striking features of the disease, and has often led to the false diagnosis of splenic anemia. It is practically always palpable, in well-marked cases extending down to the level of the navel, and occasionally reaching the proportions of a leukemic spleen, as in our Case VIII, in which it filled the entire left side of the abdomen. In a few instances no enlargement of the spleen was found, though all the other characteristics of the disease were present. In Case III of Benjamin and Shuka, the grandfather showed no splenic enlargement, while the son and granddaughter both were typical cases with very large spleens. There is therefore no reason to make a separate category out of the cases without splenic tumor.



**THE HEART.** This organ shows no abnormalities, except for a soft systolic murmur in the pulmonary area, due to the anemia.

**THE METABOLISM.** Tests for alimentary glycosuria and levuloseuria have been almost constantly negative. In our Case VII, however, a moderate excretion of sugar was noted after the ingestion of glucose, and also after levulose; it was not determined in the latter instance whether the sugar excreted was dextrose or levulose. In this same case normal values were found by one of us (Tileston) for creatin, creatinin, urea, and ammonia; the patient was on a creatin-free diet.

**COMPLICATIONS.** True gout has been associated in a few instances, notably in the family described by Murchison, and in our Cases I, IV, and XI. Articular pains, usually without joint changes, are somewhat frequently reported, and great importance has been attached to them by French observers, who make them a part of the "hepatic diathesis" ("hépatisme" of Glénard). They are not a constant feature by any means, and in our opinion have no important bearing on the disease. The various forms of chronic arthritis and arthralgia, particularly in elderly persons, are so common that it is easy to get a history of them in some members of almost any family. Urticaria is not uncommon. The complication with gallstones has already been discussed.

**PATHOLOGY.** Only eight autopsies have been performed, in the cases of Minkowski, Vaquez, Gandy and Brulé, Oettinger, Strauss, Wilson, and our Cases I and II. The cases of Strauss and Oettinger were acquired, the others hereditary; the pathological picture was the same in both types. The liver has been found normal in size, with no obstruction of the bile ducts, and no cirrhotic changes. Evidences of cholangitis have been lacking, except in our Case II, in which there were dilatation and thickening of the common duct, evidently secondary to gallstone disease. In all cases there was a considerable deposit of brownish pigment within the liver cells; this pigment contained iron in Vaquez's case, in Minkowski's it did not. In five of the eight cases stones were found in the gall-bladder. The spleen is greatly enlarged (up to 1000 grams), and usually shows signs of old perisplenitis; the increase in size is due mainly to increase of the pulp, the trabeculae being, as a rule, not much enlarged, and the follicles normal, or, as in the case of Wilson, sclerosed. Microscopically the striking feature is the marked engorgement with blood; this in one-half of the cases was most marked in the pulp, the sinuses containing little blood. There is more or less pigment in the organ, usually within endothelial cells. The amyloidosis found in our Case I was probably to be attributed not to the disease itself, but to the complication with gout. The kidneys in Minkowski's case contained a very large amount of iron, both as pigment and in combination with an albuminous body; in the other cases there was little pigment in the kidneys. The bone marrow

is found in a state of intense reaction; there is red marrow in the femur and numerous normoblasts, myelocytes, and polynuclear cells are seen.

**HEREDITY.** The disease is in most instances an exquisitely hereditary affection, frequently involving three or even four generations. It is transmitted equally by the male and by the female, and Wilson's statement that it is usually transmitted from father to daughter, and from mother to son, does not hold good for most instances. There are families in the literature in which only females are affected, and others in which the males are the ones to show jaundice. In a large series, however, the sexes are involved about equally (55 males and 45 females in 100 cases). There seems to be no racial predisposition. Some of the children almost always escape, and the offspring of those who do are always free from the disease.

**ETIOLOGY AND PATHOGENESIS.** Various theories have been propounded to account for this strange disease. Two may be dismissed from the start—the second theory of Pick, of a congenital communication between the bile passages and the lymphatics, and Hayem's latest view, that it is due to syphilis. The former is disproved by the autopsies, the latter by the entire lack of proof of the existence of syphilis in these families, and by negative Wassermann reactions in the four cases of Weber and Dorner.

The icterus present is certainly of the type known as polycholic, or, perhaps more correctly, pleiochromatic. That is to say, it is due to an excess of biliary pigment, not to obstruction of the bile ducts. This is shown by the fact that the stools are well colored, and the total urobilin output increased, as shown by Möller, and by the absence of any obstruction of the bile ducts, small or large. The presence of *temporary* obstruction of the bile ducts must be admitted for a few cases, in which with increased jaundice and usually colicky pains in the abdomen the stools became clay-colored, but these exceptions are readily explained by a complication with gallstones, which is common.

Let us next consider the first theory of Hayem, that the icterus and splenic enlargement are due to a chronic cholangitis. This view has very little in its favor, for it is difficult to conceive of a chronic infection of the bile-passages sufficient to produce jaundice dating from birth, and persisting through many years, and yet leaving no traces visible at the postmortem examination.

Minkowski believes that the disease is due to a congenital perverted function of the liver cells, by virtue of which the bile is secreted in part into the lymphatics instead of into the bile capillaries. Under normal circumstances the liver cells secrete sugar into the lymphatics and bloodvessels, and bile into the bile passages. It is easy to conceive that this selective action might be interfered with, so that part of the bile would go the wrong way. This hypothesis would account for the jaundice, but not for

the excess of bile pigment, nor for the enlargement of the spleen. Moreover, the jaundice may be explained solely on the ground of pleiochromia, for it has been shown that an excess of bile pigment is accompanied by increased viscosity of the bile, which raises the pressure in the bile passages and thus produces in a sense a mechanical obstruction to the flow of bile, and consequently jaundice.

The discovery by Chauffard of the increased fragility of the red cells threw a new light on the disease, and apparently explained the various phenomena in a satisfactory way. The red cells, being unduly susceptible to the action of hemolyzing agents, are readily destroyed, and this leads to the anemia which is so constant a feature. The bone-marrow is stimulated by the deficiency in red cells to increased activity, shown in the circulating blood by the presence of nucleated red cells and at times an increased proportion of polynuclear leukocytes, and a few myelocytes. The increased destruction of red cells leads to an increase in the material (free hemoglobin) out of which bile pigment is made, and hence to pleiochromia and icterus. Such a "hemolytic icterus" can be produced experimentally, as Lesné and Ravaut and others have shown, by the injection of hemolytic agents, which is followed by jaundice, increase in size of the spleen, and, depending upon the size of the dose, by the appearance of urobilin, bile, or hemoglobin in the urine.

Since no hemolysins can be demonstrated in the blood, the increased destruction of red cells probably takes place not in the blood, but in the spleen, that "graveyard of the red corpuscles." This leads to increased work on the part of the spleen, and hence to the progressive enlargement of the organ.

This hemolytic theory offers the best explanation of the phenomena observed, and is the one generally accepted by recent writers. The ultimate cause of the increased fragility of the red cells remains to be discovered. Two hypotheses are possible: (1) That there is a congenital defect of metabolism leading to the production of toxic substances deleterious to the red cells; and (2) that there is a congenital defect in the blood-forming organs.

**TERMINOLOGY.** As often happens in diseases of obscure causation, a multitude of names has been proposed, depending on the theory of the writer with regard to etiology, and whether the hereditary, the familial, or the congenital aspect is emphasized. For example: Chronic infectious splenomegalic icterus, chronic acholuric hereditary jaundice, congenital hemolytic icterus, chronic family cholemia, etc. Until more is known about the pathogenesis, the term chronic family jaundice may be recommended on the ground of simplicity and clearness.

**OTHER FAMILIAL DISEASES ASSOCIATED WITH JAUNDICE OR WITH SPLENIC TUMOR.** There are a few other affections which may occur in several members of a family, and show more or less resemblance to chronic family jaundice.

1. *Congenital Obliteration of the Bile Ducts.* This process, due either to congenital malformation or to inflammatory changes, leads to intense obstructive jaundice, visible at birth. It is incompatible with the long continuance of life. In some cases, however, there is only stenosis of the common duct, and the patient may live many years, with jaundice and partial decolorization of the stools; the gall-bladder is greatly dilated, from which fact and the time of appearance of the icterus the diagnosis can be made.

2. *Fatal Icterus Neonatorum without Obstruction of the Bile Ducts.* Very rarely families are met with in which almost all of the children, and they are many, become deeply jaundiced a few days after birth, and usually die within a period of days or weeks, often with convulsions. Bile is found in the urine, but the stools are well colored. Those infants which do not die early recover from the jaundice completely, but are very anemic for a while afterward. At autopsy nothing has been found to account for the jaundice; in particular there has been no obstruction of the bile passages, and no evidence of septic processes or syphilis. A curious feature is the "Kernicterus" of Schmorl; the ganglia at the base of the brain are an intense yellow, while the rest of the brain is only slightly icteric; the yellow areas show necrosis of the nerve cells. This type of icterus is peculiar to jaundice of the newborn, and has been reported chiefly in connection with the family type.

3. *Juvenile Family Cirrhosis.* Cirrhosis occurring in two or more children of a family has been described by a number of writers. A few of these cases may be attributed to hereditary syphilis, some others to the use of alcohol or other irritating substances; thus, the two children reported by Jollye (*Brit. Med. Jour.*, 1892, i, 858) both drank vinegar in large quantities. For the majority, no cause could be made out. The course resembles that of Hanot's cirrhosis, ending fatally before the twentieth year. The growth is usually stunted.

4. *Familial Splenomegaly of the Gaucher Type.* This truly remarkable disease, first described by Gaucher in 1882, is characterized by enormous enlargement of the spleen (up to 7000 grams) lasting over many years, usually occurring in several members of a family, and affecting females almost exclusively. The liver is always considerably enlarged. Anemia is seen, and brown pigmentation of the skin, but jaundice is seldom, and ascites never, present. The histological appearances are pathognomonic. The spleen, bone-marrow, lymph nodes, and in the liver the ramifications of Glisson's capsule show large numbers of peculiar cells, with small nuclei and much protoplasm. Marchand has recently shown that the large size of the cells is due to a deposit of a homogeneous material like hyaline, the nature of which could not be determined.

DIAGNOSIS. Chronic family jaundice is easily recognized, if the disease is only borne in mind. The great enlargement of the

spleen with anemia has led to the false diagnosis of splenic anemia, or Banti's disease; the latter diagnosis was made in our Case XII by a well known European clinician. The occurrence of jaundice in other members of the family, the chronicity, the early onset, the presence of bile in the feces and its absence from the urine, the changes in the blood, and the enlargement of the spleen without enlargement of the liver or indications of cirrhosis, are the important diagnostic points. From juvenile cirrhosis it is distinguished by the absence of marked enlargement of the liver, the absence of stunting of the growth, the absence of bile in the urine, and the course of the disease. Splenomegaly of the Gaucher type may be excluded by the presence of jaundice, the absence of marked enlargement of the liver, and by the fact that Gaucher's disease is familial but not hereditary. The acquired form of chronic family jaundice is distinguished from pernicious anemia by the increased fragility of the red cells in the former, and by the morphology of the blood. The frequent complication with gallstones has led to the diagnosis of jaundice due to obstruction of the common duct by calculi. This error can be avoided by attention to the above mentioned points.

**PROGNOSIS.** The prognosis is good so far as life is concerned, absolutely bad with regard to recovery. The prospects are good that some of the offspring will be free from jaundice.

**TREATMENT.** No measures have any effect on the jaundice or splenic tumor, not even the Röntgen rays. The anemia is said to have been benefited in certain cases by the use of iron, while arsenic is useless. The most that can be done is to regulate the life of the patient in such a way as to avoid the factors that tend to increase the symptoms (fatigue, excitement, indiscretions of diet, etc.). It should be realized that attacks of abdominal pain are not due to the disease *per se*, but to a complication with gallstones, and the patient should be given the benefit of modern surgical treatment, which has been neglected heretofore in all cases except VII and IX of our series.

In concluding we present the reports of thirteen cases, occurring in four families. The first of these families was investigated by Dr. Griffin, the others by Dr. Tileston. To economize space, many details have been omitted. In the urine sugar was always absent, and also acetone and diacetic acid. Urochrome was increased in all but Case XI. Albumin was absent unless otherwise specified.

*Family I. Jaundice in at least seven members in three generations. Autopsies in two cases.*

This family is remarkable for the frequency with which the condition has been associated with gallstone colic (five out of seven cases), and with gout.

**CASE I.**—O. S., male. Concerning his parents little is known, but a cousin of his father was jaundiced for many years, and suffered from severe attacks of colic. O. S. was the third of thirteen children,

ten of whom lived to grow up. One brother (H. S. S., Case II) had the same disease, and a sister was jaundiced all her life, and suffered from gallstones. O. S. was jaundiced from birth, suffered frequently from attacks of biliary colic, and died at the age of seventy-four. Of his four children, the first two were jaundiced (Cases III and IV).

*Autopsy*, May 22, 1900, Harvard Medical School, U—00—15, performed by Dr. F. T. Fulton, to whom we are indebted for the notes. There are extensive gouty lesions, consisting of marked deformity of the fingers and toes, with many sodium urate deposits (tophi) in the vicinity of these joints, and in the kidneys. The *spleen* is much enlarged, and firm; the capsule is thickened, with fibrous tags adherent. On section the trabeculae are prominent, the follicles not easily made out, the pulp not increased. The *liver* is not enlarged, of normal consistency, and on section brownish red. The *gall-bladder* is considerably distended with dark green bile, and contains 13 pigmented calculi. The bile passages are normal. There are old adhesions between the gall-bladder and the foramen of Winslow. The *kidneys* are small, granular, the capsule adherent, the cortex thinned, the pelvis dilated. The left kidney contains some cysts and a small abscess. There are also hypertrophy of the prostate, arteriosclerosis, hypertrophy and dilatation of the heart, and acute pericarditis.

*Microscopic Examination of the Spleen.* In frozen sections treated with iodine the walls of many of the smaller vessels, and certain areas closely surrounding these vessels, are stained a mahogany-brown. Sections stained in the usual way show considerable congestion, and a general increase of the interstitial connective tissue. The pulp consists of lymphocytes and red blood cells. Throughout the pulp there is considerable golden-yellow pigment, chiefly within endothelial cells. The lymphoid cells of the follicles have almost entirely disappeared, their place being taken by small pinkish masses of hyaline material (amyloid); the walls of the smaller arteries are distinctly thickened and hyaline. "The pigment is probably derived from red blood corpuscles" (F. B. Mallory).

*Microscopic Examination of the Liver.* Frozen sections show no excess of fat. With iodine the walls of the smaller interlobular vessels, and small scattered areas among the liver cells give the reaction for amyloid. There is no increase of the interstitial connective tissue, and the bile capillaries are normal. There is considerable brownish pigment within the liver cells. In minute areas the liver cells are entirely gone, their place being occupied by masses of amyloid.

*Microscopic Examination of the Kidneys.* There is a marked chronic diffuse nephritis with extensive amyloid infiltration; also an acute inflammatory process in the collecting tubules. (Ascending infection). No pigment is seen.

CASE II.—H. S. S., brother of O. S. (Case I). When first seen in July, 1903, for bronchitis, he was seventy years old. He said he had been slightly jaundiced all his life. Examination showed icterus of the skin and eyes, great enlargement of the spleen, which reached from the sixth space to the level of the navel, and a liver of normal size; myocardial insufficiency. January 4, 1904, he was seen again for a severe attack of pain in the right hypochondrium, with tenderness over the region of the gall-bladder, fever, and leukoeytosis. The stools were dark colored and the urine free from bile, while the skin was more yellow than usual. The spleen had not changed in size. This attack of cholecystitis lasted, with intermissions, for six weeks. On February 8, 1907, he was seized with his final illness, a lobar pneumonia, to which he succumbed on the 19th. An autopsy was performed by Dr. L. J. Rhea, of the Department of Pathology, of the Harvard Medical School, who has very kindly placed the notes at our disposal.

*Autopsy* U—07—18. February 19, 1907, by Dr. L. J. Rhea. The scleræ and skin have a distinctly yellowish tint. *The spleen* is markedly increased in size, and is united by firm adhesions to the diaphragm. The consistency is somewhat increased. On section it is deep red in color; the follicles are easily made out, the trabeculæ are just visible. *The liver* is apparently not larger than normal, the cut surface dark brownish red. The bile ducts stand out rather prominently. The common duct is patent. There are dense adhesions between the gall-bladder and the duodenum. The walls of the gall-bladder are thickened, and its cavity filled by a large black calculus. No stones are in the common duct or in the bile ducts within the liver. The common duct is quite markedly dilated and its walls thickened. There are also resolving pneumonia, chronic myocarditis, generalized arteriosclerosis, mural thrombi in the heart, chronic adhesive pleurisy, chronic nephritis and a persistent thymus gland.

*Microscopic Examination.* *Spleen:* The capsule is considerably thickened by dense fibrous tissue. The organ contains a large amount of blood which is in the pulp, not in the sinuses. The latter are narrow and appear compressed. Scattered throughout the organ are a few endothelial cells containing brownish pigment; some of the endothelial cells lining the sinuses, and in the capsule, contain similar pigment. *Liver:* There is a *slight* increase in the connective tissue between the columns of liver cells. The latter show quite a large amount of pigment in the form of fine scattered granules. The bile ducts are everywhere patent and their walls are not thickened. The sinusoids are moderately distended with blood and show some increase in lymphocytes, and a good many endothelial cells, which are phagocytic to red blood corpuscles, and polynuclear leukocytes. *Kidney:* There is a sclerotic process involving small localized areas.

Scattered tubules show numerous small brownish pigment granules within the epithelial cells.

CASE III.—H. B. S., aged fifty-five years, son of O. S. (Case I). First child. He has been jaundiced since birth, but the color now is less intense than formerly, having faded in the last twenty years. "Slow fever" (probably typhoid) in youth. Until he was forty he was subject to frequent attacks of gallstone colic so severe that operation was asked for, but refused by the surgeon on account of the long-continued jaundice. He has bled profusely from the left nostril at times, but does not bleed much after cuts. Feces and urine have been always dark. He has been troubled for a long time by rheumatic pains, with some deformity of the smaller joints.

*Physical Examination*, February, 1910. The skin has a yellowish tinge, evident on close inspection; the conjunctivæ are more deeply yellow. The liver is slightly enlarged to percussion and the edge is palpable on deep inspiration about two fingers' breadths below the costal margin. The spleen is enlarged to percussion and palpable at the edge of the ribs with deep breathing. *Urine*: High-colored, with deposit of urates. Bile pigment and urobilin both absent. *Blood*: Leukocytes, 13,200; moderate poikilocytosis, slight polychromatophilia. Differential count: Polynuclear neutrophiles, 80 per cent.; small lymphocytes, 13 per cent.; large lymphocytes, 7 per cent.; eosinophiles, 0 per cent. No nucleated red cells. The serum contains bile pigment (iodine test.)

R. S., the son of this patient, aged twenty-six years, has never been deeply jaundiced, though the color of his skin has always been dark. He has been subject "all his life" to attacks of vomiting, with pain in the epigastrium, sometimes in the right hypochondrium. Appendectomy done three years ago has had no influence on the attacks. Stools always colored so far as known. Examination shows nothing abnormal except a slight icteroid tint of skin and conjunctivæ. No enlargement of the liver or spleen could be made out. This case is probably one of chronic family jaundice, but in the absence of splenic enlargement and definite jaundice the diagnosis is not certain.

CASE IV.—O. A. S., aged fifty-one years. Brother of H. B. S. (Case III) and son of O. S. (Case I). Second child. He probably has been slightly jaundiced all his life, though he did not notice it until adolescence. The yellow color has never been marked, but is slightly greater during digestive upsets. Stools always brown. He has a tendency to indigestion, but there are no attacks of vomiting or abdominal pain. "Slow fever" as a boy, pneumonia at twenty-nine. During the past twenty-five years several typical attacks of pain in the great toe (gout).

*Physical Examination*, February 1910. Well developed and nourished. Skin sallow, conjunctivæ slightly yellow. *Spleen*:



Enlarged, from the sixth space to three fingers' breadths below costal margin. *Liver*: Not enlarged. No tophi.

CASE V.—M. S., aged twenty-three years. Daughter of O. A. S. (Case IV). Though always subject to "bilious" attacks with vomiting, she was never jaundiced till eight years ago, when, after typhoid fever, she began to have attacks of pain in the region of the liver, with subsequent passages of gallstones. The stools have been searched for gallstones, and about 200 have been recovered, none larger than a grape-seed. Stools always brown, urine sometimes high colored.

*Physical Examination*, February, 1910. Rather slightly built, but appears healthy. Skin and conjunctivæ slightly yellow. The *spleen* reaches from the seventh rib to the costal margin, where it is palpable. *Urine*: Bile pigment and urobilin absent. *Blood*: Red cells, 2,084,000; leukocytes, 5800. No nucleated red cells. Slight anisocytosis and poikilocytosis. Differential count normal.

CASE VI.—M. S., aged twenty-two years. Son of H. H. S. (Case II). Fifth child. He was born jaundiced, and has remained so ever since. Usually moderate, the yellow color at times becomes very conspicuous, and then he does not feel so well. Since the age of fourteen he has had "bilious" attacks about twice a year, with nausea, vomiting, diarrhœa, anorexia, and fever (up to 101.4°). Duration one or two days. *Never colic*. *Nosebleed* frequently. The stools have always been dark, the urine high-colored. The bowels move usually twice a day. The patient has been under observation since 1903, during which time there has been little variation in the condition, except that the jaundice has decreased somewhat; the size of the spleen has remained unaltered.

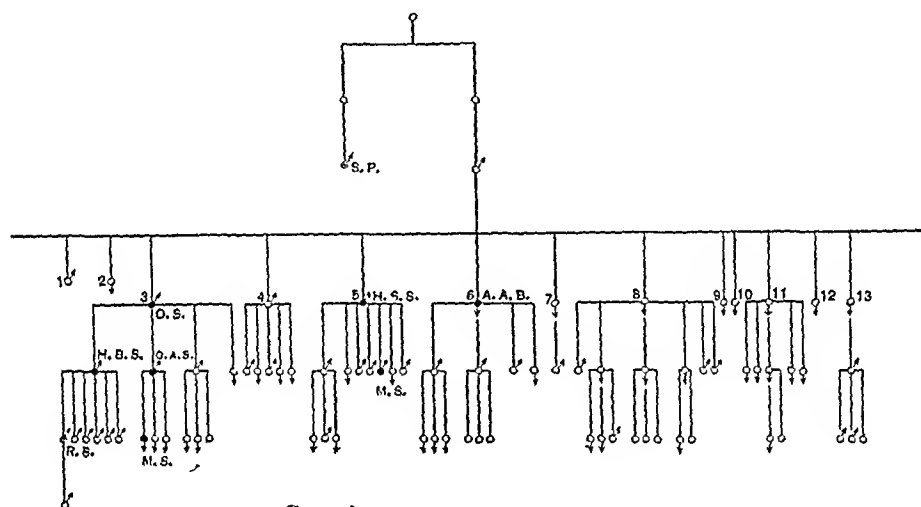
*Physical Examination*, January 23, 1910. Tall, active, slender youth (six feet two and one-half inches), weighing one hundred and sixty-eight pounds in clothes. Slight jaundice of the skin and conjunctivæ. *Spleen*: From the seventh space to level of navel, 17 cm., hard, rounded. *Liver* not enlarged to percussion, edge just palpable on deep inspiration. Heart not enlarged, systolic murmur in pulmonary area. *Urine*: Bile absent, urobilin sometimes present in traces, sometimes absent, urobilinogen in traces, urochrome abundant. Indican increased. *Feces*: Dark brown, urobilin present. Microscopically normal. *Blood*: Red cells, 4,144,000; leukocytes, 5000 and 9000; differential count normal. No nucleated red cells.

The accompanying family tree chart will serve to render more clear the relationships of the various members of the foregoing family.

*Family II. Chronic jaundice in brother, sister, and first cousin once removed.*

CASE VII.—We owe the chance to study this patient to the kindness of Dr. C. Allen Porter. W. B. W., Mass. General Hospital, No. 162,879. Aged thirty-nine years, married, no children. *Family history*: Mother died of "cirrhosis of the liver, never jaundiced"

(probably chronic family jaundice). A first cousin of mother, now forty-one years old, has been icteric since childhood. A sister of the patient, ten years older than he, was jaundiced as far back as he can remember, and had attacks of colic; she died at twenty-one years, of pneumonia. A brother, now fifty years old, has at times yellowness of the eyes, never of the skin. *Past history:* At the age of fourteen the patient noticed a yellow color of his skin, which has persisted ever since, with variations. Attacks of pain in the epigastrium with vomiting began when he was fifteen, and became more frequent and severe as he got older. In 1892 cholecystotomy and removal of 483 gallstones. The spleen was found enlarged at this time. Two later operations to close biliary fistula. Fourth opera-



Genealogical Tree of Family I.

♂ — Male and female unaffected by the characteristic.

♀ — Male and female affected by the characteristic.

— An individual with a disease which may possibly be associated with the characteristic.

○ — An individual of unknown sex.

tion in 1905, with removal of many small pigmented calculi. Since then, no further attacks of colic. The patient had bleeding hemorrhoids in boyhood, and *nosebleed* rather frequently, especially five years ago. There has been an ill-defined pain in the right shoulder ever since the last operation. Present illness, March, 1909: Has had a continual ache in the region of the spleen for several months, and feels tired and miserable. Appetite good, bowels inclined to be costive. Has had itching at times, but only of the hands and feet. A fifth operation was performed March 23, 1909, by Dr. C. A. Porter, for the cure of a hernia in the scar of the old wound, and for exploration of the biliary system. The gall-bladder was incised and contained no calculi; no obstruction of the bile ducts could be found.

*Physical Examination.* Well developed and nourished, considerable pallor. Face a peculiar buff color; the rest of the skin distinctly yellow, conjunctivæ more so. Heart slightly enlarged to left, soft systolic murmur in pulmonary area. Systolic blood pressure, 130. *Liver:* Not enlarged nor palpable. *Spleen:* Much enlarged, hard, smooth, not tender; the long axis very obliquely placed, measures 22 cm. The spleen extends from the seventh rib to the level of the umbilicus, and nearly to the middle line. *Blood:* The serum was reddish yellow and gave a strong reaction for bile. The resistance of the red corpuscles was very kindly tested for us by Dr. F. P. Gay, and a decidedly increased fragility was found. The figures for the hemolysis were as follows: 0.4 per cent. salt solution, 100 per cent.; 0.45 per cent. solution, 60 per cent.; 0.5 per cent. solution, 20 per cent.; 0.6 per cent. solution, 15 per cent.; 0.7 per cent. solution, 10 per cent. Normal blood gives little or no hemolysis with 0.5 per cent. salt solution.<sup>1</sup> There was moderate anemia, with red counts ranging from 4,400,000 to 4,116,000; hemaglobin, 80 per cent. (Sahli); color index, I. White counts, 7200 and 8100. Differential count normal. Polychromatophilia and anisocytosis present. Most of the smears showed a few normoblasts, and once an "intermediate" megalo-blast was found.

*Urine.* The urine was frequently examined, and was always of a high reddish yellow color. Urobilin was constantly present and bile pigment absent. The twenty-four-hour amount normal. Indican increased once, normal at other times. A uric acid deposit was often observed.

*Feces.* Usually one or two stools a day of a rich orange color, formed, soft, time of passage nineteen hours. Strong reaction for urobilin. During a period when Bland's pills were being taken, the stools were a deep olive-green color. This disappeared as soon as iron was discontinued, and was probably due to oxidation of bilirubin to biliverdin by the iron. A single stool, when patient was on a purin-free diet, showed a water content of 87 per cent. and normal proportions of neutral fat, fatty acids, and soaps. (Total fat, 29 per cent. of dried stool; of this, there was 38 per cent. neutral fat, 26 per cent. fatty acids, 36 per cent. soaps.)

*Stomach Examination.* No fasting contents. After Ewald breakfast hypoacidity (free HCl, 0.01 per cent.; total acidity, 0.03 per cent.)

*Bile.* Some of the bile was obtained aseptically at the operation, and examined. Cultures, both aërobic and anaërobic, made by Dr. Oscar Richardson, proved sterile. The bile was transparent, and of a deep golden-red color, evidently due to an abundance of bile pigment. Reaction neutral. No macroscopic mucus. Mucin present by acetic acid test. Bilirubin and bile acids present, albumin absent. Sediment negative.

<sup>1</sup> For the method, see Gay, *Jour. Med. Research*, 1907, xvii, 321.

*Metabolism.* In view of the present interest in creatinin, it was thought desirable to determine the amount of this substance. The patient was put on a creatin-free and purin-free diet, and after a preliminary period of three days, the urine was collected. The methods employed were, for the total nitrogen, the Kjeldahl method; for ammonia, urea, creatin, creatinin, the Folin methods; for uric acid, the Folin-Schaffer method. The determinations were made in duplicate. We are greatly obliged to Professor O. Folin for the use of his laboratory and for advice. The figures obtained are shown in the following table:

Date.	Total N. Grams.	NH <sub>3</sub> as N. Grams.	Urea as N. Grams.	Uric acid. Grams.	Creatin. Grams.	Creatinin. Grams.	Creatinin. Milligrams per kilo body weight.
April 16-17	10.81	0.60	8.63	.....	0.066	1.364	21
April 17-18	10.07	0.51	8.12	.....	0.046	1.304	20
April 18-19	9.65	0.61	7.71	.....	0.061	1.208	19
July 8-9	13.13	....	....	0.785	0.000	1.374	20

The values obtained for creatinin and urea are normal, those for ammonia are somewhat high, and the endogenous uric acid is distinctly increased. In the first period the uric acid could not be quantitated because part of the uric acid was precipitated spontaneously.

*Family III. Four members affected in three generations.*

For the opportunity to study this family we are greatly indebted to Dr. W. H. Smith, of Boston.

CASE VIII.—J. N., aged fifty-five years, of Irish descent, only child.

*Family history:* His mother was the color of saffron as long as he can remember, twenty years or more. Her three sisters were all free from jaundice. The patient has had five children; the first was a girl and escaped the disease; the second (Case IX) and third (Case X) are both yellow; the fourth, male, died at the age of seventeen months, unaffected; the fifth, also male, was born jaundiced, and died when five days old. *Personal History:* He has been jaundiced since boyhood. The color is sometimes an intense lemon-yellow, but usually only moderate. It increases after fatigue and "catching cold," but exposure to cold does not affect it. The urine has always been high-colored and the stools brown. Nose bleed during adolescence, never "bilious attacks," or itching. He often has a tired feeling, and a tendency to sleep a great deal, but his general health is better now than when he was younger. Four years ago he had an attack of tremendous pain in the epigastrium lasting several hours (gallstone colic). There were several similar attacks that year, none since.

*Physical Examination*, March 1910. Small man, height, five feet four inches; weight, one hundred and eight pounds; skin and conjunctivæ of a light yellow color; acne of face. Heart not enlarged, soft systolic murmur in pulmonary area, systolic cardiorespiratory murmur at base, venous hum in neck. Pulse, 76. *Spleen*: Greatly enlarged, reaching from the eighth rib to the level of the anterior superior spine of the ilium, and to the middle line, so that it fills the left half of the abdomen. The surface is hard, smooth, not tender. *Liver*: Not enlarged nor palpable. *Blood*: Red-cells, 3,608,000. Hemoglobin, 70 per cent. (Sahli). Color index, 1. Leukocytes, 6000. Differential count: Polynuclear neutrophiles, 77.25 per cent.; lymphocytes, 19.75 per cent.; mononuclears and transitionals, 2.25 per cent.; eosinophiles, 0.5 per cent.; mast cells, 0.25 per cent. One "intermediate" megaloblast. Anisocytosis present; average diameter (100 cells), 6.48 microns, smallest cell, 4.3, largest, 8.6 microns. No poikilocytosis nor punctate basophilia, slight polychromatophilia. *Urine*: Orange colored, slightest possible trace of albumin, bile absent, urobilin and urobilinogen present. Sediment, no casts or blood. *Feces*: Formed, color a rich golden ochre, acid. Microscopically, numerous starch granules, no excess of fat or muscle fibers; the solid particles are intensely bile-stained. Marked reaction for urobilin, traces of bilirubin.

CASE IX.—E. N., aged twenty-three years, son of J. N. At the age of eight he became jaundiced, without other symptoms. As a boy he often felt listless and suffered from nose-bleed. From the age of twelve to fourteen he had pain in the right shoulder, and at fourteen began to have attacks of typical *biliary colic*. Two years later he had 12 gallstones removed at operation; since then there has been no more colic. The jaundice deepens after unusual fatigue, and is more marked in the summer than in the winter. Minor illnesses of any sort cause an increased yellowness. There have been no "*bilious attacks*." Enlargement of the spleen was first noted in 1907, by Dr. W. H. Smith. The patient does not feel sick at all, and seems alert and active.

*Physical Examination*, February 1910. Rather slightly built, well nourished, skin and conjunctivæ a lemon-yellow color. Heart negative except for a slight systolic murmur in the pulmonary area. Pulse normal in rate. *Spleen*: Considerably enlarged, reaching from the eighth rib to 1 cm. above the navel, long axis 17 cm. *Liver*: Not increased in size. *Blood*: Red cells, 4,032,000. Hemoglobin, 70 per cent. (Dare). Color index, 0.9. Leukocytes, 13,000 at 4 P.M. The fresh blood stained with brilliant cresyl blue shows reticulation in about 10 per cent. of the red corpuscles. In stained smears there is distinct anisocytosis, with decreased average diameter (6.62 microns). No polychromatophilia nor punctate basophilia. No nucleated red cells, blood plates normal. Differential count: polynuclear neutrophiles, 71.25 per cent.; lymphocytes, 21.5 per cent.;

mononuclears and transitionals, 5.75 per cent.; eosinophiles, 1.25 per cent., mast cells, 0.25 per cent. *Urine*: Orange, bile pigment absent, urobilin and urobilinogen in large amounts. Indican not increased. Uric acid and oxalate crystals in the sediment. *Feces*: Formed, color raw Sienna, microscopically normal. Urobilin strongly positive.

CASE X—F. N., aged twenty years, daughter of J. N. For five years past slight yellowness of the eyes and skin has been noticed. Up to the age of twelve she had frequent *bilious attacks*, with vomiting of bitter stuff, lasting up to three days. Never colic or nose-bleed. The jaundice is increased by late hours and fatigue, and she gave up going to dances for this reason. It becomes more marked in hot weather. For some years she has been pale. Lately her joints are stiff, but limber up with exercise. (Stiffness probably muscular). She often has a feeling of lassitude. Otherwise she is well, except for an abnormal appetite; she does not feel satiated after a hearty meal (bulimia). The bowels usually move twice a day.

*Physical Examination*. Rather slender girl, but well developed and nourished. The slight tinge of yellow in the skin is rather becoming. The conjunctivæ appear more yellow than the skin. The heart is not enlarged; there is a soft systolic murmur in the pulmonary area. Pulse, 84. *Spleen*: Readily palpable, about 2 cm., below the ribs. *Liver*: Not enlarged. *Blood*: The serum gives a strong reaction for bilirubin. Red cells, 3,564,000. Hemoglobin, 70 per cent. (Sahli). Color index, 1. Leukocytes, 6600. Anisocytosis present, the average diameter of the red cells decreased (6.22 microns). No nucleated red cells. No poikilocytosis, polychromatophilia, or punctate basophilia; platelets normal. Differential count: Polynuclear neutrophiles, 74.75 per cent.; lymphocytes, 20.25 per cent.; mononuclears and transitionals, 3.75 per cent.; eosinophiles, 0.75 per cent.; mast cells, 0.5 per cent. *Urine*: Reddish yellow, no bile or urobilin, urobilinogen present in traces. Indican normal. Slightest possible trace of albumin, but no casts or blood. *Feces*: Soft, greenish yellow, acid. Microscopically there is an excess of neutral fat, with a few calcium soap crystals, but no excess of starch or muscle. Intense reaction for urobilin, considerable bilirubin.

*Family IV*. At least three members affected in three generations, probably several others. (Investigated through the kindness of Drs. N. A. Ludington and George Blumer, of New Haven).

CASE XI.—J. T., aged fifty-nine and one-half years, male, second child, of Scotch parents. *Family history*: His father, who died at seventy, of pneumonia, suffered from frequent attacks of vomiting of bile, lasting about a day; it is probable that his skin was yellow. Four brothers and one sister lived to grow up; one of the brothers was yellow at times, and probably had the "bilious attacks." A son of this brother is said to be sallow. The patient married his first cousin on the father's side; she is sallow and has pain in

the left side of the abdomen. She refused to be examined. Four children resulted from this marriage—two daughters who died in infancy, a son who is jaundiced (Case XII), and another son who is thought to be sallow. The patient's mother had severe arsenical poisoning while pregnant with him. *Past history:* The jaundice probably dates back to early manhood, when he began to have attacks of vomiting of bile, with headache, some pain in the right hypochondrium, and a decidedly yellow color of the skin. These attacks last two or three days, and are associated with an increase of the constipation to which he is subject. He frequently has urticaria, and used to have nose-bleed as a boy. Obstruction of the bowels at the age of twenty-two. Two years later had lead colic (occupation then, rubber-cutter.) For fifteen years he has had attacks of pain in the one or the other great toe, coming on suddenly at night. He has been a hearty eater of meat, and a beer drinker.

*Physical Examination.* Medium build, well developed, fairly nourished. Skin yellowish; face of a sallow, leathery color; conjunctivæ distinctly yellow. No lead line. The lungs show signs of emphysema. The heart is moderately enlarged to the left, with soft systolic murmurs at the apex and at the aortic area. Aortic second sound rather sharp. Subclavian arteries thickened, radials not. Pulse, 80; systolic pressure, 165 to 170. *Spleen:* Greatly enlarged, measuring 12 by 17 cm., not tender. Liver flatness from fifth rib to costal margin, where the edge of the organ is palpable. Distinct thickening about metatarsophalangeal joints of both great toes. No tophi. *Blood:* Red cells 2,804,000. Hemoglobin, 50 per cent. (Tallqvist). Color index, 0.9. Leukocytes, 7900. Moderate anisocytosis, average diameter normal (7.64 microns). No nucleated red cells. No achromia, poikilocytosis, polychromatophilia, or basophilia. Differential count: Polynuclear neutrophiles, 80.6 per cent., lymphocytes, 15.7 per cent.; mononuclears and transitionals, 2 per cent.; eosinophiles, 1.7 per cent. Urine of normal color; specific gravity, 1009; albumin, a slight trace; no bile or urobilin; a faint trace of urobilinogen present. Indican normal. In the sediment fairly numerous hyaline casts; no blood (chronic interstitial nephritis).

The complication with gout is of interest, but in the presence of lead poisoning and the overconsumption of meat and malt liquors is not surprising.

CASE XII.—G. T., aged thirty-two years, son of J. T. The permanent yellow color was not noticed until ten years ago, but was probably present before that. Since the age of seventeen he has had "*bilious attacks*," in which he would feel tired, drowsy, and depressed, with jaundice, constipation, and headache, and toward the close of the attack vomiting of bile, or *nose-bleed*. Several such attacks in a year, lasting a day or two. They seem to be brought on by constipation, fatigue, or irregular hours of eating. Light attacks without vomiting once every two weeks. When twenty years old

had a severe cramp in the epigastrium, doubling him up, and occasionally since then he has had similar attacks. (*Cholelithiasis*.) He has *hives* frequently, to which an occasional itching of the legs may be attributed. Appetite good, sleeps "unusually well." Stools always dark, "like chocolate." He is said to have had malaria eleven years ago, but had no chills; at that time a doctor found the spleen enlarged. Two months ago a prominent European consultant made a diagnosis of Banti's disease.

*Physical Examination.* Medium-sized man, sparsely nourished. The skin of the body is a pale lemon-yellow, while the face is of a peculiar brownish-yellow, leathery color, unlike the hue of ordinary jaundice. The conjunctivæ are distinctly jaundiced. Heart not enlarged, slight systolic murmur at base. Pulse normal. *Spleen:* Greatly enlarged, measuring 22 x 13 cm., reaching below to the level of the spine of the ilium and to the middle line at the navel. It is smooth and hard, and tender at one point. *Liver:* Palpable at costal margin, area of dullness normal. *Blood:* Serum strongly tinged with bile, and gives a marked Hedenius reaction. Red cells, 3,492,000. Hemoglobin, 65 per cent. (Tallqvist). Color index, 0.9. Leukocytes, 5800. Two normoblasts seen. Marked anisocytosis, average diameter decreased (6.48 microns). No achromia, slight poikilocytosis, some polychromatophilia, no punctuate basophilia, except in one normoblast. Platelets normal. Differential count normal. *Urine:* Orange, contains urobilin and urobilinogen, but no bile. *Feces:* Mushy, yellow (milk diet), alkaline. Numerous hreds resembling connective tissue. Microscopically normal except for increase in the calcium soap crystals. Urobilin strongly positive, bilirubin absent.

*Stomach examination* after Ewald breakfast: 40 c.c. undigested bread mixed with mucus, free HCl 0, total acidity 5, slight test for lactic acid (chronic gastritis).

CASE XIII.—C. T., aged seven years, son of the foregoing patient, grandson of J. T. The eyes have been yellowish since birth. The color becomes more apparent when he is constipated. He has had no children's diseases, only frequent colds. Nose-bleed once, never colic or vomiting attacks, except after eating strawberries or bananas. Hives frequently. The child has seemed healthy, but never could run like the other boys, and complains of a pain in the left side of the abdomen after exercise. Appetite and digestion good, bowels regular as a rule, sometimes constipated.

*Physical Examination:* March, 1910. Well developed for his age, and well nourished. He is the least jaundiced of this family, but the skin and conjunctivæ are distinctly though faintly yellow. On the legs, arms, and scrotum a few wheals, one on the scrotum showing hemorrhagic infiltration. Mucous membranes somewhat pale. Heart not enlarged, loud systolic murmur in pulmonary area and venous hum in neck, pulmonic second sound not accentuated.



*Spleen:* Much enlarged, measuring 18 by 13 cm., smooth, not tender. *Liver:* Slightly enlarged; dulness above at sixth rib; liver palpable 3 cm. below costal margin. *Blood:* The serum on standing shows a green fluorescence and is strongly positive for bile pigment. Red cells, 3,412,000. Hemoglobin, 50 per cent. (Sahli). Color index, 0.74. Leukocytes, 8500. Two normoblasts and one "intermediate" megaloblast seen. Marked anisocytosis, average diameter decreased (6.69 microns). Considerable achromia and poikilocytosis, some polychromatophilia, and very fine punctate basophilia. *Urine:* Somewhat high colored, no bile, urobilinogen absent, urobilin in traces. Indican normal. *Feces:* Formed, dry, yellowish brown, alkaline, microscopically normal. Urobilin present, but reaction with zinc acetate less intense than in the other cases. Bilirubin absent.

An interesting point in this family is the tendency to urticaria, which is present in all three generations.

The bibliography which follows makes no pretence at completeness. Only those articles are included which could be personally verified, hence some foreign references have been omitted. The French literature on the subject is very voluminous, owing to the fact that the same case may be reported twice by different observers, and that some authors feel it necessary to write many articles on the subject. Many such references are purposely omitted.

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## A STUDY OF MURMURS IN PULMONARY TUBERCULOSIS.

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Two things in particular prompted the present study in regard to murmurs: (1) Their frequency and wide distribution in pulmonary tuberculosis, especially in far advanced cases; and (2) the difficulties in diagnosis they may occasion. The clinical records in a number of cases of pulmonary tuberculosis have been investigated in regard to murmurs, and the results tabulated. The term murmur has been used in the restricted sense of a sound possessing more or less of a blowing or whiff-like character, and not in the comprehensive sense, which "includes all those adventitious acoustic phenomena connected in some way with the heart's action, and not resembling in tone the normal cardiac sounds" (Babcock).

The cases have been divided into two groups: (1) Those in which there is some gross lesion of the heart or bloodvessels—for instance, endocarditis or myocarditis; and (2) those without any such lesion definitely diagnosed, and usually without any clearly defined cause. The second group will be considered first. All cases are to be understood as belonging to this second group except when the contrary is specifically stated.

Murmurs independent of demonstrable changes in the heart or bloodvessels occurring in tuberculosis have received attention from time to time since Stokes described a murmur in the subclavian artery. Some authors, for instance, Walshe, Wilson Fox, and Samuel West, devote a small space to these murmurs; others, as Cornet, barely refer to them. From the opinions expressed one concludes that murmurs of this sort are not limited to tuberculosis, in fact, may occur in normal individuals; that they are heard rather infrequently; that they are apt to be temporary and to be modified by the phases of respiration; and that their causes cannot be definitely determined. These murmurs are usually described as occurring most frequently at the base of the heart or in the subclavicular regions, less often at the apex, over the back, and elsewhere.

Uniform statistics on the frequency and distribution of murmurs are not to be expected because of the variable factors on which murmurs often depend. Some of these factors are exertion, sudden or protracted, the position of the patient, the character of the breathing, the stage of the disease, the frequency of examination, the quietness of the examining room (a very important factor in hearing the fainter murmurs), the natural acuity and the training of the examiner's ear, and the degree of concentration employed in ausculting. Statistics on the frequency of murmurs in pulmonary

tuberculosis are available from comparatively few sources. At the Henry Phipps Institute<sup>1</sup> functional murmurs occurred in 3.4 per cent. of 2078 cases, distributed as follows: Systolic at the mitral area, 36 (1.73 per cent.), and systolic at the pulmonic area, 35 (1.67 per cent.). At the Adirondack Cottage Sanitarium,<sup>2</sup> where most of the cases are not far advanced, functional murmurs occurred in 6 per cent. of 1289 cases. These murmurs were divided about equally between the base (chiefly the pulmonic area) and the apex.

The occurrence of murmurs over the chest was investigated in 80 cases of pulmonary tuberculosis, in which it was impossible to ascribe the cause to any gross cardiac or vascular disease. The great majority were females—63, in contrast to 17 males. There was 1 case under ten years of age, there were 9 cases between ten and twenty years, 38 between twenty and thirty years, 18 between thirty and forty years, 7 between forty and fifty years, and 7 cases were over fifty years of age. In other words, there was nothing specially interesting about their ages. Most of the cases were far advanced—61, in contrast to 9 incipient and 10 moderately advanced cases. Examinations were made repeatedly in most of the cases, and were usually conducted in an absolutely quiet room.

FREQUENCY AND DISTRIBUTION OF THORACIC MURMURS IN 80 CASES (NOT DUE TO DEMONSTRABLE CARDIAC OR VASCULAR DISEASE).

	Cases.
Murmurs present . . . . .	56
Both anteriorly and posteriorly . . . . .	25
Anteriorly . . . . .	22
Posteriorly . . . . .	9
Murmurs anteriorly . . . . .	43
Both sides . . . . .	17
Right side . . . . .	7
Left side . . . . .	19
Murmurs on the right side, anteriorly . . . . .	23
Both above and below third rib . . . . .	12
Above third rib . . . . .	8
Below third rib . . . . .	3
Murmurs on the left side, anteriorly . . . . .	36
Both above and below third rib . . . . .	21
Above third rib . . . . .	6
Below third rib . . . . .	9
Murmurs in the axilla . . . . .	10
Both axillæ . . . . .	1
Right axilla . . . . .	4
Left axilla . . . . .	5
Murmurs posteriorly . . . . .	34
Both sides . . . . .	8
Right side . . . . .	11
Left side . . . . .	15

<sup>1</sup> Henry Phipps Institute, Fifth Annual Report.

<sup>2</sup> Lawrason Brown, AMER. JOUR. MED. SCI., December, 1908.

THE FREQUENCY AND DISTRIBUTION OF THE MURMURS. Murmurs were audible over the chest in 56 of these 80 cases. According to the stage of the disease, murmurs were present in 3 of the 9 incipient cases, 8 of the 10 moderately advanced cases, and 45 of the 61 far advanced cases. Murmurs were audible both anteriorly and posteriorly in 25 cases, anteriorly alone in 22 cases, posteriorly alone in 9 cases. Anteriorly, murmurs were present on both sides of the chest in 17 cases, on the right side alone in 7 cases, and on the left side alone in 19 cases. Over the sternum, murmurs were recorded in 24 cases. On the right side of the chest, in front, murmurs were present both above and below the third rib in 12 cases, only above the third rib in 8, and below in 3 cases. On the left side, in front, murmurs occurred both above and below the third rib in 21 cases, only above the third rib in 6, and below the third rib in 9 cases. Murmurs anteriorly were audible in the different interspaces in the following number of cases:

	Right side. Cases.	Left side. Cases.	Sternum. Cases.
First interspace . . . . .	10	12	5
Second interspace . . . . .	20	26	13
Third interspace . . . . .	13	20	14
Fourth interspace . . . . .	7	19	12
Fifth interspace . . . . .	5	18	9
Below fifth interspace . . . . .	1	1	2
Not stated . . . . .	0	0	1

Posteriorly, murmurs were present on both sides in 8 cases, on the right side alone in 11 cases, on the left side alone in 15 cases. Murmurs were heard in both axillæ in 1 case, in the right axilla alone in 4 cases, and in the left axilla alone in 5 cases. In all the cases in which the murmur was audible in the axilla one could also be heard in some other part of the chest, and usually the axillary murmurs were topographically continuous with those audible elsewhere.

For practical purposes, many of the murmurs may be advantageously classified according to limited areas over which they are heard with the greatest intensity; for example, the base of the heart, the region of the apex, the region of the angle of the scapula, etc. Some murmurs, however, do not have any very limited area of maximum intensity.

In my experience, murmurs over the front of the chest occur most frequently at the base. They are generally heard in the second interspace, more often in the left than the right, or at the same level over the sternum. Laterally, they usually extend only a short distance from the sternum, particularly on the right side. Murmurs at the base may have a wider distribution, but under these circumstances it is often difficult to determine whether we are dealing with two or more murmurs running together or overlapping. In 37 of the 80 cases a murmur was audible in the right or left second

interspace, or at a corresponding level over the sternum, most of these covering quite limited areas.

Murmurs were heard about half as often at the apex as at the base. Their maximum intensity was at, or a little inside, the cardiac apex, usually in the fifth interspace, between the parasternal and midclavicular lines; less often in the fourth interspace. They were rarely transmitted beyond the anterior axillary line, even when they seemed pretty clearly due to mitral regurgitation (mitral regurgitation not dependent on gross cardiac disease). In 4 of these cases the situation, transmission, loudness, and persistency of these murmurs seemed to indicate leakage at the mitral valve.

Systolic murmurs over the sternum, below the level of the fourth rib, occurred in 13 cases. They were usually faint, and sometimes were transmitted from other regions. Sufficient evidences on which to base a diagnosis of tricuspid regurgitation, particularly the presence of a positive venous pulse, were lacking in all the cases. In only 1 case was anything heard suggestive of the xiphosternal crunching sound.

The murmurs on the left side, anteriorly, covered larger areas, as a rule, than those on the right side. Out of 36 cases with murmurs on the left side, the murmurs were limited to a single interspace (usually the second or the fifth) in 13 cases, to two interspaces in 6 cases, to three interspaces in 5 cases, to four interspaces in 5 cases, to five interspaces in 6 cases, and to six interspaces in 1 case. In no case was a murmur limited to the axilla. Apical murmurs were transmitted to the axilla in 3 out of 6 cases with axillary murmurs.

Posteriorly, murmurs were recorded in 34 of the 80 cases, eight times on both sides, eleven times on the right side alone, and fifteen times on the left side alone. A murmur may be heard over a very limited area or over the whole of the back of the chest. While the latter is rare, it is common to find a murmur covering a considerable portion of one or both sides of the back. But in nearly every case, irrespective of the extent of the murmur, an area of maximum intensity will be found at or near the angle of the scapula, close to the angle of the scapula or below it, or inside it, or over the lower portion of the interscapular region. In only 1 case were two points of special intensification recorded on one side, posteriorly—a case in which the murmur was audible all over the left side, posteriorly, but specially marked above the spine of the scapula and at the angle of the scapula.

Murmurs may occur over very limited or over extensive areas. In 1 incipient case a murmur could at times be heard over nearly the entire chest. Murmurs entirely distinct from one another may be heard in different parts of the chest in the same individual as at the base and at the apex, or may blend together and prevent outlining the exact limits of a murmur.

Only murmurs over the chest have been referred to. Adventitious sounds above the clavicles are not infrequent in tuberculosis; sometimes they are murmurs of a blowing or whiff-like character, but more often only a roaring, humming, or rumbling sound is heard.

**TIME OF THE MURMURS.** Systolic murmurs were present in all of these 56 cases. It was sometimes impossible to tell with absolute certainty the time of the murmurs over the back of the chest. Out of the 56 cases, a diastolic murmur was recorded in only 4, and in 2 of these cases only once after several examinations. All the diastolic murmurs were associated with systolic murmurs, and were of the same character. In 3 of the cases the murmur occurred over some part of the sternum and the left side adjacent, and in 1 the murmur was audible on the right side from the second to the fifth interspace, inclusive, and from the sternum to the midclavicular line, and very faintly for a short distance beyond. The last occurred only on inspiration. In 1 of these cases at one examination there could at times be heard a faint diastolic murmur in the left interscapular region. In 3 of the cases the murmur was rough. In all the cases the second aortic sound was, at least at times, accentuated.

In a case not included in the above series a very extensive diastolic murmur, not dependent on any demonstrable cardiac or vascular disease, was encountered in a woman, aged twenty-eight years, with extensive left-sided pulmonary and pleural involvement, the heart being apparently slightly retracted upward and to the left. Her hemoglobin was 80 per cent. The diastolic murmur was audible over the sternum from the second interspace to the sixth rib, and extended beyond the left midclavicular line, reaching the anterior axillary line at the level of the fifth rib. The maximum intensity was in the third interspace, at the parasternal line. There was also audible a systolic murmur over a part of this area and over a part of the right side. The time and distribution of murmurs varied on different occasions.

**INTENSITY OF THE MURMURS.** Faint murmurs were described in 33 out of 48 cases in which the intensity of the murmurs was mentioned. Sometimes they were very faint, an occasional one being audible only with a Bowles stethoscope. In 1 case, a murmur could be heard with an ordinary stethoscope and not with the Bowles. To hear some of these murmurs, absolute quiet in the room and concentrated attention were necessary. In some patients murmurs could be heard on only one of several examinations, and sometimes specially favorable circumstances, as a certain position of the patient, excitement, exertion, etc., were required.

In 15 cases a murmur was described as distinct, fairly loud, loud, or marked. In 4 cases there was quite a marked systolic murmur at the apex. The base, the apex, and the regions of the angles of the scapulæ were the most common seats of the louder murmurs and of the maximum intensity of murmurs of wide distribution.

Fairly loud murmurs, as a rule, covered only small areas, but were more apt to be extensive posteriorly than anteriorly. Various factors, like exertion, that may produce murmurs, may also increase their intensity. The different phases of the respiratory act may have quite a marked effect on the loudness of a murmur. Like murmurs due to endocarditis, these murmurs may vary greatly at different examinations.

**LENGTH OR DURATION OF THE MURMURS.** The length of the murmurs was shorter than often occurs with murmurs due to other causes, like endocarditis, but the rate of the heart was nearly always increased. The only case in which a fairly prolonged murmur was recorded was an incipient case, with a normal heart rate.

**THE QUALITY OF THE MURMURS.** The murmurs were generally soft and blowing in character, sometimes being heard as very faint whiffs. Occasionally a slightly ringing quality was audible. In only 3 cases was a rough murmur recorded, in 2 cases the roughness affecting both the systolic and the diastolic murmurs. Rough murmurs were audible only anteriorly.

While murmurs in advanced cases may vary from time to time in loudness, extent, etc., they usually do not entirely disappear, and when they do it is generally only temporarily. This persistency we have noticed especially in regard to murmurs at the apex and over the back.

**RELATION TO RESPIRATION.** In 36 cases the relations of the murmur to inspiration, expiration, and the respiratory pause were recorded. While most of the murmurs could be heard during all parts of the respiratory act, they were usually louder at one portion than at another. The commonest time for diminution or cessation of murmurs was during inspiration, except at the very end of inspiration. In 10 cases the murmur was inaudible during inspiration. In but 1 case a murmur was stated to have been heard during inspiration only. When murmurs were modified by respiration the greatest intensity usually took place during expiration, or during expiration and the respiratory pause, sometimes at the end of inspiration and beginning of expiration.

The effect of holding the breath was recorded in 16 cases with murmurs. In only 2 cases did the murmur disappear when breathing was suspended. As a rule, the murmurs were heard equally as plainly when the breath was held as during the act of respiration. In 2 cases a murmur could only be heard when breathing was suspended; in 1 of these cases only after expiration. Occasionally a murmur would weaken after the breath had been held for some time.

The relative weakness or absence of murmurs during inspiration in many of the cases, I believe, was often due to the loudness and sometimes to the exaggeration of inspiration. Inspiration is normally louder than expiration, and is apt to become intensified over



healthy tissue when such tissue is reduced in amount. Thus, murmurs are apt to be heard over one base at the back when the opposite side is extensively infiltrated, and the loudness of inspiration under such circumstances is quite sufficient to obscure a faint murmur.

In only 3 cases did the character of the murmurs suggest that they might be due to the passage of air through normal or abnormal channels, instead of their being circulatory in origin. Such murmurs may have been caused oftener, but we could not demonstrate this. Rarely distinct respiratory puffs, synchronous with the heart beat, occurred. Occasionally it may be difficult to distinguish between a murmur and a rale.

**RELATION TO BODILY POSITION.** Most of the 80 cases were examined in a sitting position during the ordinary routine chest examination, but a small proportion were also auscultated while standing or while lying down. Occasionally the position of a patient modified the murmur, but it was generally less the position than the attending exertion that seemed responsible for the modification. In advanced tuberculosis it takes very little effort to cause or to modify murmurs. Sometimes one position will reveal a faint murmur; the same position later, after the patient has been listened to in various other positions, may reveal a much louder murmur. Or the reverse result may be observed. For instance, a murmur audible just after a patient takes his seat, may disappear after this position has been maintained for some time. With the murmurs at the apex, the sitting position was more apt to be associated with the presence of a murmur or its intensification than the horizontal position. Very few records were made of examinations with the patients in the right or left lateral positions.

**RELATION OF MURMURS TO THE KIND OF UNDERLYING LUNG TISSUE, WHETHER HEALTHY OR DISEASED.** In advanced tuberculosis, murmurs are usually louder or more widespread, and occur oftener over the functioning lung tissue than over the diseased portions, with the possible exception of the left side in front. Thus, in 10 cases with a murmur on the left side posteriorly, and none on the right, there was considerable healthy tissue on the left side, especially at the base, and much less or none at all on the right side. Likewise, in 8 cases with a murmur at the right base posteriorly, more healthy tissue was found here than at the corresponding situation on the left side. In a boy, aged two years, a murmur was audible over the right back when the left side was extensively diseased. Murmurs were also more frequent over the right side, in front, when the tissue here was healthy than when it was diseased. When there was not much lung involvement on either side, however, murmurs were more frequent or were louder or more widespread at the left base posteriorly, than at the right, in our cases in the proportion of 6 cases on the left to 1 case on the right—an occurrence not peculiar to tuberculosis.

**ETIOLOGY.** The attempt to determine the causes of these murmurs in any given case is usually met with great difficulties. Any factor proposed to explain their occurrence will often be wanting in cases with murmurs, or may be present even when murmurs are absent. Even in cases in which murmurs can be produced artificially, for instance, through exertion, one can, as a rule, only venture an opinion as to their complete etiology. The subject is further complicated by the occurrence of murmurs in apparently normal individuals.

Murmurs associated with tuberculosis and with other forms of marked debility probably often depend on similar causes, the exact nature of which, however, is usually obscure. The determining cause in some of the cases is doubtless contraction or imperfect expansion of the great vessels, resulting from adhesions, enlarged glands, pulmonary consolidation, displacement of the heart, and an enlarged heart pressing on bloodvessels. According to Thayer and MacCallum,<sup>3</sup> only very slight pressure over the pulmonary artery or conus arteriosus, in dogs, results in the development of a systolic thrill and murmur immediately beyond the point of pressure. If murmurs in the pulmonary artery are produced as easily, relatively, in man as in dogs, traction or pressure upon this vessel may readily explain some of the murmurs audible at the base of the heart. Some of the murmurs may be ascribed to roughening of the aorta or to slight roughening or thickening of the valves of the heart. The frequency of the latter condition is shown by the figures of Norris;<sup>4</sup> who found endocardial thickening in 15 per cent. of 1764 autopsies on tuberculous patients, the proportion of valvular involvement being: mitral, 183; aortic, 126; tricuspid, 23; and pulmonary, 13. A congenitally small aorta, said to be not infrequent in tuberculosis, suggests a possible cause for some of the murmurs. West considers that the murmurs at the angle of the scapula may often be due to air being forced out of lung tissue by the cardiac pulsations. It seems possible that murmurs audible over a large part of one healthy lung when the opposite lung is extensively involved may be due to circulatory changes in the pulmonary artery on the unaffected side. The marked persistent murmurs at or near the apex are probably quite often due to leakage at the mitral valve, the result of weakness of the mitral sphincter or the papillary muscles. Similar conditions affecting the tricuspid valve may cause some of the murmurs heard in the lower sternal region. A moderate oligochromemia occurs frequently in tuberculosis, not oftener, however, in cases with murmurs than in those without. We have been unable to demonstrate any constant relationship between the transmission of murmurs and pulmonary consolidation near their seat of origin. In many cases

<sup>3</sup> AMER. JOURN. MED. SCI., February, 1907.

<sup>4</sup> Ibid., October, 1904.

on such relationship exists, and in some, especially those with murmurs situated posteriorly, consolidation seems to interfere with their transmission. The proportion of cases with murmurs increases with the advance in the disease, and for their explanation one naturally looks to the conditions peculiar to advanced cases, particularly as they affect the circulatory system. Some of these conditions are quite constant, for instance, an increase in the pulse rate and a fall in blood pressure; others are more variable, like the strength of the heart beat. But it is impossible to find any relationship between these circulatory conditions and the occurrence of murmurs constant enough to warrant definite conclusions as to causation; and, least of all, is it possible to demonstrate any etiological relationship in individual cases. It is not surprising that slight exertion or excitement produces or modifies murmurs in weak advanced cases in which various circulatory factors, for instance, the rate of the heart, are so easily upset by even trivial causes.

In the maze of questions brought up by this subject one would fain take comfort in what has been said by Sahli, that the difficult problem is not to explain why murmurs do sometimes occur, but rather why, with all the conditions apparently favorable for their production, they do not always occur.

**DIAGNOSIS.** A diagnosis as to whether a murmur is due to endocarditis or to other causes may be made very difficult, even impossible, by the presence of advanced pulmonary tuberculosis. Such difficulties have been most frequently occasioned, in our experience, by systolic murmurs at the apex. With these apical murmurs we have to determine whether mitral regurgitation is present or absent, and, if regurgitation is present, to determine whether it is due to endocarditis or not.

In advanced cases of pulmonary tuberculosis with presumable cardiac weakness, fairly loud systolic murmurs at or near the apex, transmitted toward the axilla, and heard repeatedly over a considerable length of time, may, in the majority of cases, be strongly suspected of being due to leakage at the mitral valve. These murmurs are usually only faintly transmitted beyond the midclavicular line, and are rarely audible in the axilla. They are unaccompanied by demonstrable enlargement of the heart, or by any apparent general effect, and are interesting chiefly for the uncertainty in diagnosis they may occasion.

Difficulty in determining whether a murmur, supposedly due to mitral regurgitation, occurring in advanced pulmonary tuberculosis, is due to endocarditis or not may arise because tuberculosis and heart disease have so many manifestations in common. Cyanosis, dyspnoea, curving of the nails, accentuation of the second sound at the pulmonary cartilage, a murmur at the angle of the scapula, are common in both heart disease and pulmonary tuberculosis. The effect of position on the murmur has been too variable, in our

experience, to be of much real help. The all-important evidence, that a mitral regurgitant murmur is due to endocarditis, namely, enlargement of the heart, may be difficult to obtain in tuberculosis because of the difficulty to locate the position of the apex, and to determine the cardiac outlines by percussion. Uncertainty as to the location of the apex may be due to a very feeble apex beat, or to a diffuse one dependent on an overacting heart. The location of the apex and the percussion outlines may give unreliable information, on account of the presence of compensatory emphysema, retraction of the lung, consolidation adjacent to the heart, and cardiac displacement. However, when the heart is drawn to the left, the maximum apex impulse is frequently in the fourth interspace, and in no case do we recall a maximum apex impulse to have occurred downward (sixth or seventh interspace) and outward in a heart itself normal.

A definite history of acute articular rheumatism furnishes corroborative evidence in favor of endocarditis, while a history simply of rheumatic pains is of little value, as they occur so frequently in tuberculosis.

With the appearance of failing compensation the peculiar features of this condition should be sought for, as they are apt to furnish quite a contrast to what is encountered in tuberculosis. Marked pulsation and dilatation of the cervical vessels is common in the later stages of heart disease, but is uncommon even in advanced tuberculosis, except for the prominence of the veins that may be seen during the act of violent coughing. Cyanosis is often more pronounced in failing compensation than in advanced tuberculosis. Pulsation from an enlarged liver is frequently met with in the final stages of failing compensation, an unknown occurrence, in our experience, in uncomplicated tuberculosis. On account of the great rarity of the typical evidences of failing compensation in cases very far advanced in tuberculosis, if, indeed, they ever appear under these circumstances, their occurrence furnishes evidence of the strongest kind in favor of the presence of some causative condition in no way associated with tuberculosis.

Myocarditis due to valvular disease and various causes of a non-tuberculous nature often exhibits certain features that are uncommon in cases of tuberculosis even when they are advanced. Thus, marked irregularities may occur within a short period in the force of the heart beats, or in the duration of individual cardiac cycles. A typical example is a case in which the heart beats weaken at irregular intervals, and are accompanied by a corresponding intermission of the pulse. Another example is found in cases with delirium cordis. These abnormalities, moreover, do not necessarily follow any regular sequence or depend on any temporary or removable cause. In tuberculosis, on the other hand, the irregularities are apt to be limited to variations in rate, or to the

interpolation of additional sounds, such as occur in reduplications, the cardiac rhythm, as a whole, not being affected. Sudden and marked variations in rate are frequently met with in tuberculosis, but are often due to some temporary cause, like excitement, and disappear on its removal. In tuberculosis abnormal cardiac sounds are common, but the length of individual cardiac cycles and the force of the heart beats only rarely show marked and irregular variations. When these variations do occur they often depend on some temporary and removable cause. We refer, of course, to sounds during a limited time, for instance, during one examination, and not to variations that may occur from day to day or from week to week.

Other murmurs due to endocarditis or to congenital cardiac defects seem of less practical importance diagnostically than the mitral regurgitant murmurs, either because of their infrequency or because of the greater readiness with which a diagnosis may usually be made. Unlike mitral regurgitation, the other common forms of valvular disease, mitral stenosis, and aortic regurgitation have certain distinctive features, the former especially the peculiarity of the thrill and murmur, and the latter especially the evidences outside of the heart. Moreover, these features are not likely to be obscured by the associated tuberculosis.

Endocarditis was recorded in 0.9 per cent. of 71,000 cases of pulmonary tuberculosis collected by Lawrason Brown.<sup>5</sup> A positive diagnosis of endocarditis was made in 2 cases, and a probable diagnosis of endocarditis in 1 case, out of 171 consecutive cases of pulmonary tuberculosis at the Home for Consumptives at Chestnut Hill. There were 32 incipient, 44 moderately advanced, and 95 far advanced cases; 41 were males and 130 were females. Doubtful cases were examined repeatedly over considerable periods of time. No cases of pericarditis, of congenital cardiac defect, or of vascular disease other than arteriosclerosis were diagnosed in this group of cases. Myocarditis was strongly suspected in a number of cases; particularly advanced ones, but I must admit that we have rarely been able to furnish scientific evidence of this condition in uncomplicated tuberculosis.

CASE I.—This patient is a young woman, aged twenty-seven years, single. Her occupation has been ordinary housework. At twelve years of age she had pneumonia, and since then her health has never been completely restored. At fifteen she had rheumatic pains in all her limbs. At sixteen she had measles, and the same year developed an anal fistula. At nineteen she had typhoid-fever and pleurisy: the latter recurred several times later. The duration of the tuberculosis is considered to have been between eight and fifteen years. Her height is five feet one and a half inches, and her weight

<sup>5</sup> AMER. JOUR. MED. SCI., February, 1909.

110 pounds. The sputum contained tubercle bacilli on the last examination. The urine contains no albumin. The hemoglobin is 75 per cent. The diagnosis of the pulmonary condition is arrested incipient tuberculosis.

*Heart.* The apex beat is usually diffuse, reaching beyond the left midclavicular line in the fourth and fifth interspaces. A pre-systolic thrill is usually present at the apex. Deep percussion gives dulness above at the second rib, on the right at the right border of the sternum, and on the left a short distance beyond the midclavicular line. The second pulmonic sound is at times accentuated. There is always present a prolonged presystolic sound, usually a rumble, sometimes a whiff-like murmur, over an area varying in size in the fourth and fifth left interspaces near or at the apex. Less often, there is a systolic murmur in the region of the apex, sometimes reaching as far as the anterior axillary line, promoted more by exertion than by position. The patient enjoys moderate, though not vigorous, health, except for occasional attacks of gastric disturbance, accompanied with marked palpitation and dyspnea. At these times there may be marked arrhythmia of the heart, even a mild grade of delirium cordis, suggesting myocarditis, though; ordinarily, compensation is fairly well maintained.

*Diagnosis.* Endocarditis of the mitral valve, with mitral stenosis and, to a less extent, mitral regurgitation; moderate cardiac hypertrophy.

CASE II.—M. C., female, aged fifteen years, single, has been attending school irregularly. She had a typical attack of acute articular rheumatism at six, and has never been as well since. Her history of tuberculosis dates back seven years, when she had an attack of pleurisy. She is five feet in height and weighs 90 pounds. There is no albumin in the urine, the hemoglobin is 88 per cent. The most extensive involvement is on the left side. While this is a far advanced case, the patient is steadily improving, and leads a pretty active life.

*Heart.* The apex beat is diffuse, the most marked impulse being in the left midclavicular line, in the fifth interspace. There are no thrills. The upper border of cardiac dulness is at the third rib, the right border at the right border of the sternum, and the left border a short distance beyond the midclavicular line in both the sitting and horizontal positions. The pulmonic second sound is accentuated. When the patient is sitting there is a constant, distinct, fairly loud, blowing systolic murmur, most marked in the fifth interspace at the midclavicular line, transmitted into the left axilla, audible to the right as far as the parasternal line, and disappearing above at the junction of the latter with the third rib. It is much fainter in the horizontal position. Faint systolic murmurs are audible at the inferior angle of the scapulæ, the more marked one on the left side.

*Diagnosis.* Endocarditis of the mitral valve, with mitral regurgitation; moderate cardiac hypertrophy; compensation good.

CASE III.—J. F. B., male, aged forty years, married, travelling salesman by occupation, had nothing of importance in his family history, except that his maternal aunt had died twenty-five years before of consumption. He had scarlet fever at seven, but gave no history of rheumatism. His mother states that he began to have "spells," accompanied with unconsciousness, at twelve, and that he has always been a little odd. He stated that he had a heart attack at twenty, and that occasional attacks of fainting had occurred since. For a number of years he had been subject to copious hemorrhages from the bowels, and he had suffered from stomach trouble. Five months before admission he had had a violent cold, something like whooping cough, accompanied with severe dyspnoea, which had never left him. The duration of the tuberculosis had apparently been at least five months. His height was five feet six and one-half inches. His weight was 129 pounds, only 10 pounds loss in the previous five months, though twelve years previously he had weighed 154 pounds. The sputum showed tubercle bacilli before admission, none on two examinations subsequently. The urine showed a trace of albumin, many casts, which later increased in number; red cells also appeared later. Hemoglobin, 90 per cent. There was marked cyanosis, and the dyspnoea, with air hunger, was so severe that he could hardly rest at all at night. There was marked pulsation of the cervical vessels. There was enlargement of the liver and œdema of the lower extremities, which later increased. The extent of the tuberculosis in the chest was difficult to determine, but apparently this was a moderately advanced case.

*Heart.* There was a distinct heaving impulse in the fifth and sixth left interspaces, reaching in the latter situation nearly to the anterior axillary line. There was no thrill, but an uncertain presystolic impulse. The heart extended upward to the upper border of the third rib; on the right, a finger's breadth beyond the right border of the sternum; and to the left, nearly to the anterior axillary line. A systolic murmur was audible in the fifth and sixth left interspaces, from the sternum into the axilla, being most marked in the sixth interspace beyond the midclavicular line, in which location it was quite loud. It entirely disappeared before death. The first sound at the apex was weak and muffled and of very poor muscular quality. For a time it was almost entirely replaced by the murmur. Sometimes a long presystolic rumble was audible at the apex. The pulmonic second and aortic second sounds were never accentuated. Posteriorly, a systolic murmur was heard below the left scapula. The cardiac rhythm was usually fairly well preserved; at least, the individual cardiac cycles did not show much variation. The patient died at the end of seventeen days. The diagnosis of the heart lesion was probable endocarditis of the mitral

valve, mitral regurgitation, cardiac hypertrophy, myocarditis, and failing compensation. It was impossible, however, to exclude as the cause of the regurgitant murmur myocarditis in a heart hypertrophied in consequence of an antecedent nephritis.

**SUMMARY.** Murmurs over the chest not demonstrably dependent on cardiac or vascular disease, when listened for carefully, under favorable circumstances and repeated examinations, are found frequently in tuberculosis. They were heard in nearly three-fourths of our advanced cases. These murmurs are usually systolic in time and faint in intensity, in our cases three-fourths being faint. They are generally soft and whiff-like in character, though they may be quite loud and harsh. In the majority of cases these murmurs are heard repeatedly, and usually intermit only temporarily. The areas where they are most commonly heard, and where their maximum intensity most often occurs, are at the base of the heart, chiefly to the left of the median line, at the cardiac apex (a little over half as often as at the base), and at the inferior scapular angles posteriorly, more often on the left side. These murmurs are more frequent over the front of the chest than the back; they are more frequent and more widely distributed over the left side in front than the right. They are heard in a relatively small number of cases in the axillæ. They may be very limited in extent or may cover nearly the entire chest. In our cases the murmurs were usually heard best during the quietest part of the respiratory act, that is, during expiration or the respiratory pause, and during suspended respiration; less often they were limited to the end of inspiration and beginning of expiration, and rarely they were heard during inspiration only. These murmurs are modified at times by position, more often by excitement and exertion. With the possible exception of the left side in front, murmurs in advanced cases are heard more frequently over normal or hyperfunctionating tissue than diseased tissue, this being particularly noticeable at the bases posteriorly. The etiology of these murmurs is usually obscure, and causes probably responsible in a certain proportion of all cases are hard to establish in individual cases. In about 7 per cent. of our cases with murmurs, mitral regurgitation dependent on weakness of the heart muscle was diagnosticated. For prognosis and treatment, little is gained from these murmurs of undetermined origin. Even when they seem to depend on the advance of the tuberculous process they furnish little information unobtainable in other ways.

The diagnosis between cases with murmurs due to gross cardiac disease and those without any such cause demonstrable may be rendered very difficult in the presence of pulmonary tuberculosis, especially if it is far advanced. Tuberculosis has many symptoms found in heart disease, and often renders the physical signs of the heart inconclusive, in particular making the size of the heart difficult



to determine. The apical murmurs, in our experience, most frequently occasion uncertainty in diagnosis.

Out of 171 cases of pulmonary tuberculosis (over one-half being far advanced cases, and nearly three-fourths being females), a diagnosis of endocarditis was made in 2 cases (mitral regurgitation once, and mitral regurgitation and stenosis once), and a diagnosis of probable endocarditis (mitral regurgitation) was made in a third case. That is, endocarditis was diagnosticated in 2 or 3 of 171 cases. In none of these cases was a diagnosis of disease of the pericardium or of the aorta made. Myocarditis is not infrequently demonstrated microscopically in hearts from persons dying of tuberculosis, and its occurrence is often suggested clinically. The diagnosis, however, in individual cases of tuberculosis is usually very difficult, first, because of the frequent absence of important signs, for instance, certain types of arrhythmia; and, second, because many of the symptoms of myocarditis may also be produced by tuberculosis. Heart disease with failing compensation I have never met in very far advanced tuberculosis.

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## TWO CASES OF SOLITARY FALSE NEUROMA—PROBABLY NON-MALIGNANT.

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FROM time to time there are reported cases of solitary tumors developing in nerves. Most of them are of small size and are composed of fibrous tissue. Sometimes the nerve fibers are easily separated from the tumor. At other times they form an integral part of its substance or are lost in the tissue of which the tumor is composed.

Within a year it has been my fortune to operate upon two patients suffering from a serious form of fibrous tumor affecting the nerves. As such condition is not adequately described in any one of a dozen well-known text-books on surgery and pathology which I have consulted, the details of these two cases seem worth recording.

CASE I.—The first patient, M. S., came to me from Dr. Tukey, of Bridgeport, and Dr. Dougal Bissell, of New York. He was a young man, aged seventeen years, with an excellent family and personal history. Two years previous to my first examination he fell on the sidewalk while running, and struck his head so that he was unconscious for nine hours. His right shoulder and left leg were badly

bruised. In two weeks all symptoms had disappeared. Fourteen months after this accident there was noticed a swelling of the back of the left leg. This increased for about a year, and, according to his parents, it remained stationary afterward. There was absolutely no pain nor any disability. He had grown rapidly—gaining twenty-five pounds in six months.

Physical examination of the patient, made February 7, 1909, showed him to be an unusually well-developed young man, five

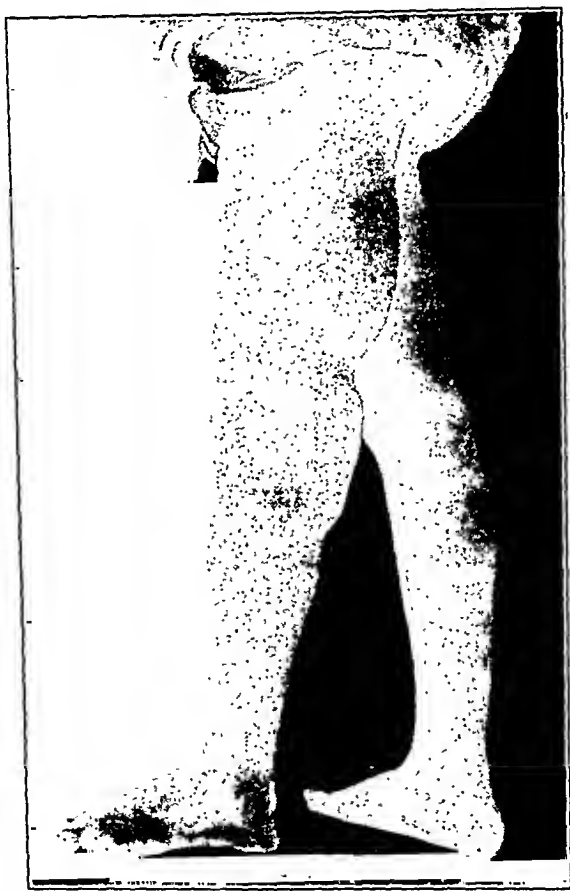


FIG. 1.—Fibrosarcoma of the deep fascia of the thigh and leg involving the sciatic nerve and some of its branches.

feet and ten inches in height, weighing one hundred and sixty-seven pounds. The lower half of the left thigh and the left knee measured from three to four inches more in circumference than the corresponding parts of the right limb. This difference was due to a hard, elongated swelling situated in the back of the thigh and leg. It was not attached to the overlying skin, but closely attached to the deep fascia. Its lower portion presented a distinct rounded outline; but the upper margin was lost beneath the deep muscles on the back of the thigh (Fig. 1). The whole tumor measured about sixteen

inches in length and five inches in width. It was so narrow in the fold back of the knee that it was difficult to say whether or not the portions in the calf and thigh were connected. Pressure upon the tumor produced no unpleasant sensation. There was a slight venous enlargement in the overlying skin, but there was no enlargement of the inguinal or other lymphatic glands.

A diagnosis of fibroma or an encapsulated sarcoma was made, and an immediate removal of the tumor (or tumors) was advised.

Operation was performed February 21, 1909, with the assistance of Drs. Bissell and Tukey. An incision was made directly down-



FIG. 2.—Portion of the tumor situated in the calf, after its removal. In the groove shown at the left of the picture lay the external branch of the popliteal nerve. At this level the internal branch of the popliteal nerve was wholly in front of the tumor.

ward from the popliteal space for a distance of six inches. Numerous enlarged veins were divided and ligated. The tumor was covered by deep fascia, to which it was not adherent. It was intimately attached to the fascia covering the gastrocnemius muscle. The external branch of the popliteal nerve was partially surrounded by the tumor, but was not attached to it. Finally, the whole of the tumor below the fold of the knee was cut from its deep attachments. Part of the aponeurosis of the gastrocnemius muscle had to be removed with the tumor. The latter was continuous with the mass in the thigh by an isthmus one and one-half inches wide and one inch thick. This was cut square across, and the lower portion of the tumor was removed. The wound was closed by suture and healed primarily.

The portion of the tumor removed measured four and one-half by five and one-half inches, and weighed nineteen ounces (Fig. 2). It was entirely composed of dense white fibrous tissue. It cut like sole leather. Dr. F. M. Jefferies, who made the pathological examination, reported it to be a fibrosarcoma (Fig. 3).

Three weeks later, assisted by Drs. Tukey and Roberts, of Bridgeport, I made an attempt to remove the remaining portion of the tumor in the thigh. The whole posterior surface of the tumor was exposed and the upper and lower portions of it were removed, as well as portions to the right and left of the sciatic nerve, but the main trunk of this nerve lay in the centre of the tumor and was so intimately connected with it as to be indistinguishable from the tumor itself.

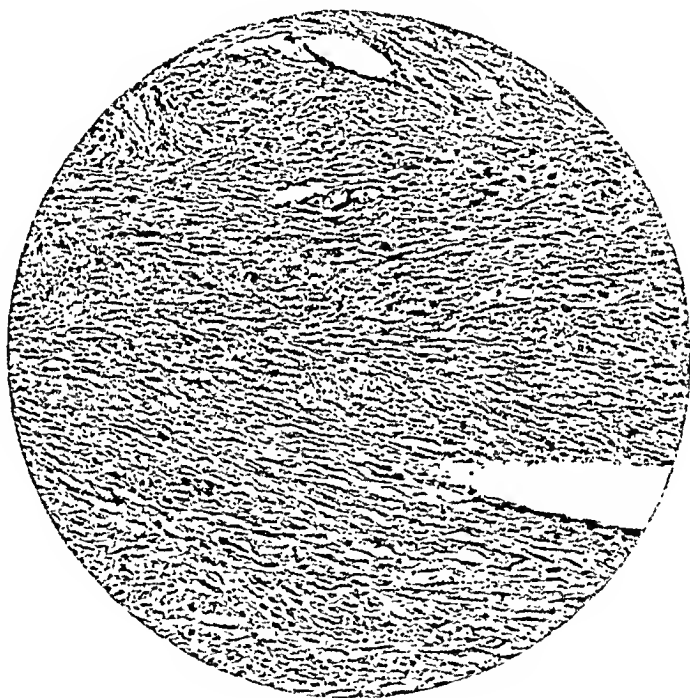


FIG. 3.—Tumor of the thigh involving the sciatic nerve ( $\times 200$ ).

The complete removal of the tumor, therefore, would have meant the sacrifice of the sciatic nerve. To this the parents would not consent. The wound was sutured and healed without difficulty. There was no paralysis of the muscles of the leg or foot. The only nerve injury at the operation was the cutting of a few small branches of the sciatic in the thigh.

November 21, 1909, the patient wrote me that the upper and lower part of his left leg measured the same as the right; that the centre of the thigh, where a portion of the tumor was left, was one inch larger in circumference than the right; and that there was no pain or discomfort in the leg. He said it felt just the same as the right

one, and that he never knew that he ever had trouble with it. He walks from three to five miles a day to and from school, dances, runs, and enjoys the best of health, never favoring himself in any way. He weighs one hundred and ninety pounds, a gain of twenty-three pounds since the operation. The flesh is hard and the muscle is the same in both legs. On April 13, 1910, his health was still perfect.

CASE II.—J. L. McM., a man, aged thirty-eight years, well developed and of previous good health, noticed twenty years ago a small swelling on the top of the right shoulder. There was no history of injury. This swelling remained small for eleven years, and then gradually grew until it was prominent above and below the right clavicle and well backward toward the cervical spine. It was painless until six months previous to his entrance to the New York Skin and Cancer Hospital, July 28, 1909. Since that time it caused him so much pain in the arm and shoulder that he finally had to give up work.

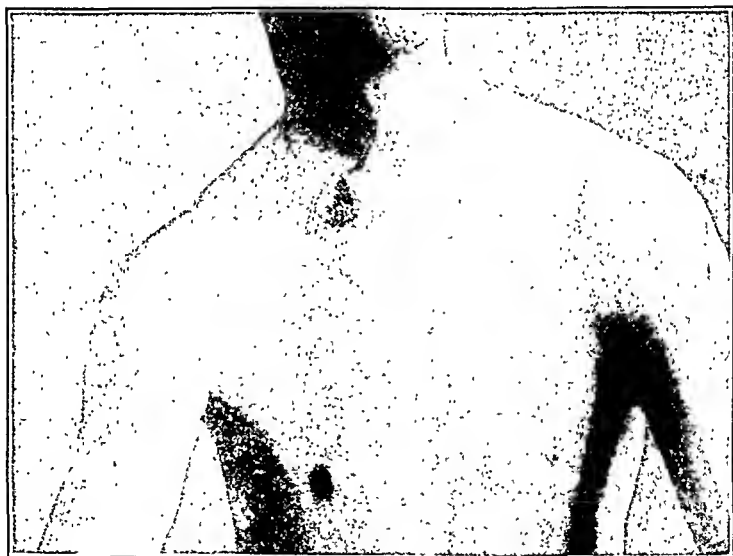


FIG. 4.—Fibroma of the brachial plexus, right side.

Physical examination showed a hard, immovable, rather nodular mass, close to the right side of the sternum, but extending nearly to the coracoid process and backward along the base of the neck nearly to the spine. The most prominent part of the mass was about the sternal articulation of the clavicle. It was covered by normal movable skin (Fig. 4).

Operation, July 29, 1909. An incision was made from the upper end of the sternum outward a distance of five inches and the tumor exposed. It was found to lie between the pectoral muscles and the ribs. It was intimately attached to both these structures, so that in dissecting it from the greater pectoral muscle it was necessary to

sacrifice a part of the latter; and to remove the tumor from the bones to which it was attached it was necessary to take away some of the periosteum. In spite of this intimate attachment it did not infiltrate the surrounding tissues after the manner of the usual forms of sarcoma, and the edges of the tumor were rounded and fairly distinct. Large portions of the tumor were dissected free and cut away until the cords composing the brachial plexus were exposed. The tumor was composed of dense, white fibers, which cut like sole leather. Toward the axillary margin of the tumor it was possible to distinguish it from the nerves which come from the brachial plexus. Toward the centre of the tumor the nerve trunks were apparently fused in the tumor in such a manner that they were indistinguishable.

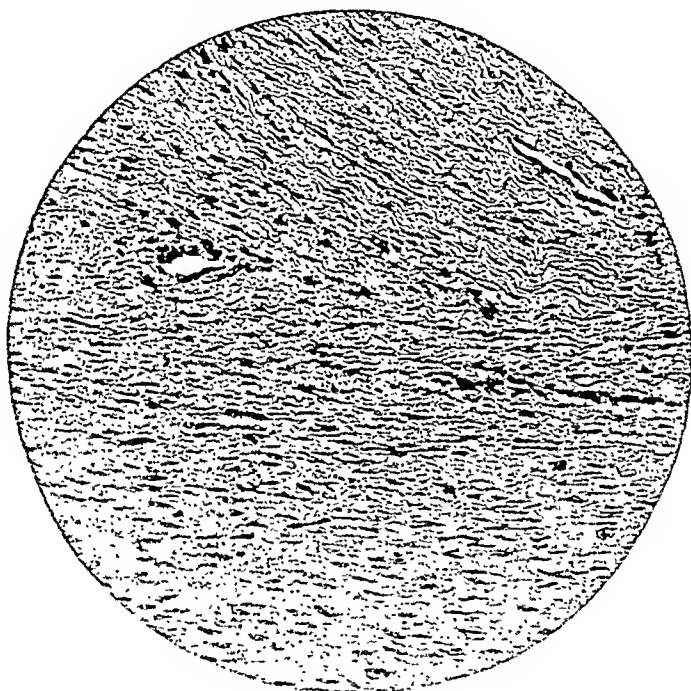


FIG. 5.—Tumor of the neck involving the roots of the brachial plexus ( $\times 200$ ).

To have removed the whole of the tumor would apparently have meant removal of the brachial plexus. A considerable portion of the tumor—probably more than half of it—was therefore left in position and the wound was closed. The patient was at once relieved of his pain. Tests of the motions of the arm made on the following day showed that there was no paralysis. The wound healed primarily. The sutures were removed August 5.

Pathological examination was made by Dr. H. H. Janeway, who pronounced the tumor a fibroma durum (Fig. 5).

November 15, 1909. Examination of the patient showed that there was little apparent increase in the size of the portion of the tumor

remaining, but the patient stated that for some weeks he had noticed pains in his arm at intervals and that their frequency and severity was on the increase.

December 2. Portions of the tumor were removed from above the clavicle through two incisions, one in the front and one in the back of the neck. In both instances the portions of the tumor removed were apparently connected with the deep cervical nerves, although the fibers could not be traced through the tumor. They seemed to lose themselves in its substance. The portion of the tumor removed from the back of the neck was closely adherent to the upper angle of the scapula. The patient made a good recovery from his operation, still retaining the various motions of his arm. He was for a time entirely free from pain.

January 24, 1910. He complained of pain between the upper angle of the right scapula and the median line. The arm was weak, though all motions could be made.

February 10, 1910. Pain was less severe, and the patient had gained seven pounds in weight.

March 25, 1910. He reported that his general health was good, that the arm was still weak, and that for a few nights he had a severe pain from the shoulder to the end of his fingers, lasting only a limited time.

These tumors offer so much that is interesting, that Dr. Janeway kindly made additional sections of both of them for comparison. He reported as follows: "I have cut sections from both tumors and believe them both to be fibromas. Sections from Case II gave no suggestions whatever of nerve tissue. The tumor is composed of abundant intercellular fibrous bands, in the meshes of which are branching connective tissue-cells of such a degree of development that it is impossible to consider them sarcomatous. The tumor from Case I has exactly the same structure, with the exception that the cells are even less sarcoma-like and the amount of intercellular fibrous tissue is greater. This tumor was very hard indeed, and it was very difficult to get thin sections from it. It is surely a mistake to consider either tumor sarcoma; and in this Dr. James Ewing, who also examined the tumors, agrees. It is true that local recurrence is possible, and in these cases almost certain, because of the impossibility of removing all the tumor tissue; but one need not fear metastasis unless the original tumor changes its character. In regard to the origin of these growths there are two possibilities. Either they originated from the connective tissue nerve sheaths, or the fascia external to the nerve sheaths and involved the nerves secondarily."

Since tumors of this character do not form metastasis, the outlook after complete removal is extremely good. Unfortunately, these two were so placed that their complete removal meant the loss of the use of a limb. I believe that the first patient should have

an amputation about six inches above the knee-joint. This would enable one to remove the tumor even though it extends as high as the sciatic foramen, and still leave a sufficient amount of material to cover the bone and form a serviceable stump. I so advised the patient, but his family would not consent to it.

In the second case complete removal of the tumor would necessitate amputation of the arm at the shoulder-joint, since it would probably be necessary to ligate and remove the axillary artery and vein as well as all the roots of the brachial plexus. I have hesitated to offer this advice until it is definitely shown that the palliative effects of the operation are only temporary.

I have been unable to find reported any cases exactly like these two. For the sake of comparison extracts from a few published cases are here mentioned, since they have some points of similarity with the two which are the subject of this sketch.

R. W. Smith<sup>1</sup> in his *Treatise on the Pathology, Diagnosis, and Treatment of Neuroma*, one of the most beautiful monographs that has ever been published, described the case of John McC., aged thirty-five years, who was admitted in 1840 to Richmond Hospital. He had a large tumor on the right side of his neck which existed for fifteen years without having caused the patient any pain. Three years later he was again taken to the hospital complaining of pain due to a large tumor in the back of the left thigh (Fig. 6). Subsequently, numerous small tumors developed in the peripheral nerves, and the patient died a few months later. Careful examination of all the nerves of the body showed that there were 1400 tumors growing in them, which were removed and counted. In the left sciatic and its branches there were more than 200. These tumors were recognized as being malignant, although at that time (1843), of course, no microscopic examination was made. The large tumor in the neck was associated with the right pneumogastric.

Herczel<sup>2</sup> reports a case somewhat similar to my second one, in which he removed by dissection a tumor involving the brachial plexus both above and below the clavicle. A new growth was disposed along some of the nerves of the plexus in a series of nodules more or less bead-like, and in places fused together. There was in no place any indication that the nerve fibers themselves had a part in the tumor formation. The tumor was a fibroma, showing in places myxomatous degeneration. It was combined with diffuse elephantiasis of the arm. The removal of this tumor produced paralysis of the biceps, brachialis anticus, and supinator longus muscles, with some loss of power in the flexors of the fingers. The tumor recurred after removal, especially in the forearm. In the skin of the upper arm there had been from birth an elevated, pig-

<sup>1</sup> A Treatise on Pathology, Diagnosis, and Treatment of Neuroma. Dublin, 1849.

<sup>2</sup> Beit. z. path. Anat. u. z. allg. Path., 1890, iii, 38.



mented area. This also increased in size. At the last observation, made nearly two years after operation, the paralyzed muscles had markedly atrophied. Otherwise the condition was about the same.

Hume<sup>3</sup> removed from a man, aged twenty-four years, six inches of the sciatic nerve with a tumor which involved it and extended from the gluteal fold to the popliteal space. In a month the patient was able to walk without support. All the muscles below the knee

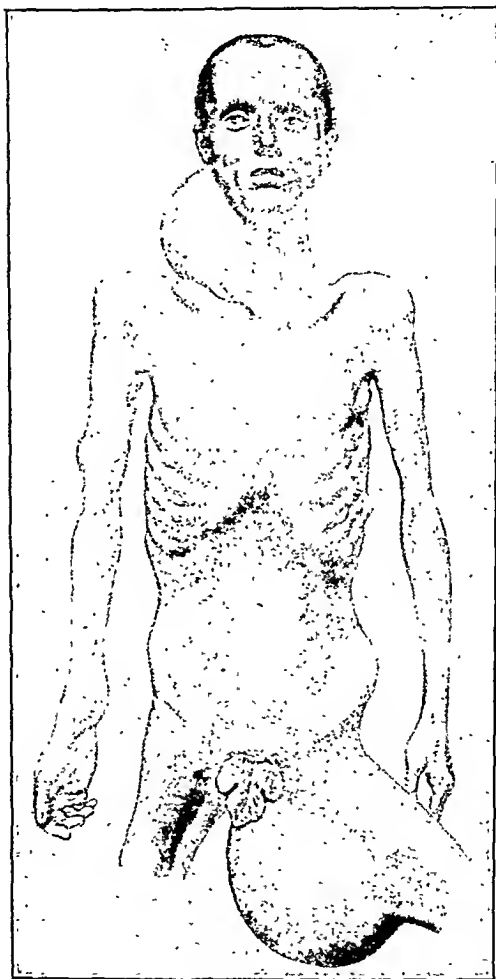


FIG. 6.—Multiple neuromas (case of R. W. Smith).

were paralyzed, and the patient used his leg like a flail, swinging it forward by means of the extensors of the knee. In another case he removed a tumor of the sciatic nerve from beneath the gluteus maximus of a man aged thirty-seven years. In this case it was possible to stretch the nerve sufficiently to effect a partial suture of the portions left by the resection of the nerve and tumor. Six months

<sup>3</sup> Lancet, 1891, ii, 654.

later he walked very well, being able to flex the leg on the thigh, but not to move the foot on the leg. The tumor in each case was a sarcoma.

Buchanan<sup>4</sup> mentions a case of tumor of the internal popliteal nerve. The tumor was about five inches long and completely filled the popliteal space. There was no paralysis or oedema of the leg. Amputation was performed through the thigh. The upper limit of this tumor was just below the division of the sciatic into internal and external branches. The sheath of the internal branch was stretched over the tumor and formed its capsule. On section strands of nerve fibers could be seen passing through the tumor growth. The tumor was soft and grayish in color, very vascular, and showing in places yellowish degenerative spots. The external popliteal nerve lay above the surface of the tumor, and was not involved in it.

Our knowledge of tumors of the peripheral nerves may be said to have begun in the year 1811, when Odier<sup>5</sup> suggested the name neuroma for "larger, movable, circumscribed, and deeply placed tumors, which are characterized by painful swelling of the nerves involved." It was not, however, until 1829 that an Edinburgh physician, named Wood,<sup>6</sup> accurately described the gross anatomy and symptoms of these tumors. He recognized the fact that they are composed chiefly of the connective tissue which surrounded the nerve fibers and not of the nerve fibers themselves.

Virchow<sup>7</sup> made an attempt to classify the various tumors connected with nerves, which up to that time were all included under the name neuroma. He distinguished between true neuroma, a tumor made up of new-formed nerve fibers, and false neuroma developing from the sheath of a nerve. He classed among the true neuromas the bulbous swellings often seen in the ends of the nerves of an amputation stump; but at the present time pathologists do not count these as tumors at all, since the various twisted nerve fibers which they contain are only a continued growth of the normal nerve fibers which have been cut across at the time of amputation. The division suggested by Virchow has been amplified by later investigators. For the sake of those who wish a complete classification, the following table is reproduced from Bruns<sup>8</sup> book on *Tumors of the Nervous System*.

<sup>4</sup> Brit. Med. Jour., 1900, i, 955.

<sup>5</sup> Manuel de la médecine pratique, Genève, 1811.

<sup>6</sup> Observations on Neuroma, Edinburgh Med.-Chir. Transactions, 1829, iii, 367.

<sup>7</sup> Die Krankhaften Geschwülste, Berlin, 1863.

<sup>8</sup> Die Geschwülste des Nerven-Systems, Berlin, 1908.

Neuromas	True	Neuromas containing ganglion cells.	The occurrence of true neuromas without ganglion cells is doubtful.
	False	<ol style="list-style-type: none"> <li>1. Circumscribed or solitary tumors which spring from connective tissue of the nerve trunks or from that of the ganglia in connection with nerves.</li> <li>2. Diffuse overgrowth or multiple nodules of the connective tissue of nerves and their ganglia. Neurofibromatosis.</li> <li>3. Dejerine's interstitial hypertrophic and progressive neuritis of infancy.</li> <li>4. Thickenings of the nerves occurring in tuberculosis, leprosy, and syphilis.</li> </ol>	<p>Benign (Fibromas, myxomas, cysts, etc.).</p> <p>Malignant (The various forms of sarcoma, also fibrosarcomas, myosarcomas, and cystic degenerated sarcomas.</p> <p>(a) Circumscribed or diffused and generalized fibromatosis of the nerve trunks.</p> <p>(b) Plexiform neurofibromatosis.</p> <p>(c) Neurofibromatosis of the skin (mollusum fibrosum).</p> <p>(d) Elephantiasis neuromatosis.</p> <p>(e) Malignant changes taking place in the tumors grouped under a, b, c, or d.</p>

I believe that the tumors which form the basis of this article belong in the benign or possibly the malignant group under division 1 of the false neuromas. The question may properly be raised whether they are nerve tumors at all. The fact that the edges of both tumors were found growing in fascia clearly outside of the nerve sheaths is the one point against such classification. But toward the centre in each case the relation of tumor to nerves was as intimate as it could possibly be. For purposes of both diagnosis and treatment, and for prognosis too, they are certainly tumors of the great nerve trunks. Whether they are such etiologically cannot perhaps be definitely proved unless an opportunity is had to dissect their deeper older parts.

These solitary peripheral neuromas may occur at any age; but according to Courvoisier<sup>9</sup> they are usually preceded by some traumatism. In the days of bloodletting the wound caused by this was often the starting point. The median nerve is oftenest affected; then the ulna, the sciatic, and the radial. The predominance in the upper extremity may be due to the more frequent traumatism of the hand and arm. The large majority of tumors do not exceed an inch in diameter. The very large ones are usually malignant. One diagnostic point for all neuromas is the fact that the tumor is movable from side to side and not in the direction in which the nerve runs. The benign tumors grow very slowly, often requiring decades to reach any considerable size. The malignant tumors may or may not grow rapidly. They show their malignancy by breaking through the outside sheath of the nerve and growing into the surrounding tissues, especially into the muscles. They may also spread farther into other tissues and set up metastasis in the same manner as malignant tumors starting in other structures of the body.

In strictly benign cases the nerve fibers often escape injury, so

<sup>9</sup> Die Neurome: Ein klinische Monographie, Basel, 1886.

that no symptoms are produced. This may also happen with malignant growths, but in that case there is likely to be at least pain. The pain may be very intense, and usually comes on in attacks. It is described as boring, sticking, burning, or like an electric shock. Changes in position, variations in temperature, and other slight causes may bring on these attacks. Sometimes by pressure the tumor causes pain in an adjacent healthy nerve. Other nervous manifestations are paresthesia, symptoms of motor irritation, anesthesia, and very rarely motor paralysis. Kölliker<sup>10</sup> says disturbances in sensation are more common than disturbances in motor power. Trophic disturbances rarely occur.

The diagnosis in multiple cases is usually easily made; in cases with a single tumor it is more difficult, unless the pressure of the tumor has given rise to some paresis, or unless direct pressure upon it produces symptoms of irritation in some nerve trunk.

If one has decided that a neuroma exists involving certain nerves, it is important to know whether the tumor grows from (a) the sheath of the nerve, the epinurium, or (b) the perinurium, which surrounds the smaller bundles of nerves, or (c) the endonurium, which surrounds the nerve fibers. In the first case the tumor may lie wholly outside of the nerve. Its removal under such circumstances is, of course, much easier, and may be accomplished without severing the nerve; but unfortunately this can only be decided by an operation.

A differential diagnosis between benign and malignant tumors can often be made. Slow growth is indicative of a benign tumor. Rapid growth, or rapidity of growth after traumatism, in the case of a long-standing tumor, suggests malignancy. Severe nervous attacks, anesthesia, and paralysis suggest malignancy. Other signs of malignancy are recurrence after operation in the same or in other nerves, infiltration of the surrounding tissues rendering the tumor immovable, involvement of the lymph glands or metastasis elsewhere, and ulceration of the overlying skin.

The prognosis in benign cases is good, but if it is necessary to cut the nerve to remove the tumor, even though it be sutured afterward, a guarded prognosis must be given. In the malignant cases prognosis is bad, but even in such cases a long time may elapse before a fatal termination is reached. Bruns mentions a recurrent neuroma in the sciatic five years after the removal of a similar tumor from one of the nerves of the foot. The tumor of the sciatic was removed, and the patient was free from recurrence fifteen years afterward. Other similar instances might be mentioned. In non-malignant cases prognosis is bad if there are multiple painful tumors. A patient so afflicted becomes cachectic, whereas in cases without pain he may live for many years.

When the diagnosis has been established it is by no means easy

<sup>10</sup> Deut. Chirurgie, 1891, Lief, 243.

to decide upon the form of treatment to be adopted. If the tumor is situated upon a small nerve leading to the skin the question of paralysis need not be considered; whereas, if it is upon an important nerve trunk the possibility of permanent injury of the nerve must be borne in mind, even in strictly benign cases. If the pain is intense, it may be better to run the risk of paralysis, or even deliberately to produce a paralysis, rather than to allow the patient to suffer repeated painful attacks. Indications for operation in malignant tumors are, of course, much stronger. The decision then will turn chiefly upon the possibility of a complete removal of the tumor.

The four forms which operation may assume are: (1) Extirpation of the tumor without division of the nerve; (2) extirpation of the tumor with resection of the nerve; (3) amputation of the limb; (4) neurotomy or stretching of the nerve involved. The choice of operation will depend in part upon whether the tumor is malignant or not and in part upon its relation to the nerve trunk. Hence the first thing to do is fully to expose the tumor; then, unless it is evidently of a malignant character, its relation to the nerve fibers should be ascertained, either by splitting its capsule or by splitting the tumor itself. If the tumor is so fortunately situated as to leave intact the whole or a large portion of the nerve, it can be removed without permanent injury. In the case of malignant tumors the same rule should be followed here as elsewhere and the incision made wide of the growth. The question of amputation of the limb will depend partly upon the nerve or nerves involved and partly upon the existence of metastasis. If a radical operation is impossible, but pain is intense, it may be possible to divide the affected nerve on the proximal side of the tumor.

If the tumor is a benign one, and yet its removal necessitates resection of the nerve, it may be possible to restore the continuity of the nerve by suture. Hume attempted this in one of his cases, and succeeded in obtaining voluntary control of part of the muscles supplied by the divided sciatic. Possibility of restoration of sensation after suture of the nerve is, of course, greater than restoration of motion. This is especially true after suture of the median and other nerves of the arm. The anastomosis of fibers of the different nerves permits a partial restoration of function, which makes it very difficult to estimate the effect of a nerve suture in the arm. Primary restoration of nerve function after suture in the sense of primary union of a wound is absolutely unknown. Courvoisier called attention to the fact that recurrence after extirpation does not often take place, even in cases in which amputation has been performed for malignant tumors of nerves. One evil effect of operation which was formerly rather common was tetanus; with the cleaner surgery of today this need not be feared.

## REVIEWS.

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A HANDBOOK OF MEDICAL DIAGNOSIS. By J. C. WILSON, A.M., M.D., Professor of the Practice of Medicine and Clinical Medicine in the Jefferson Medical College, Philadelphia. Pp. 1435; 422 illustrations. Philadelphia and London: J. B. Lippincott Company, 1909.

Professor Wilson's *Handbook of Medical Diagnosis* is an ambitious volume: it is large in size, larger than any other in the English language, and comprehensive in scope. It is divided into four parts, of which the first treats of medical diagnosis in general, medical topography, the examination of the patient, and case-taking; the second, of the methods of diagnosis and their immediate results, including physical diagnosis, laboratory diagnosis, as well as examination of the eye, and the use of the  $x$ -rays; the third, of the symptoms and signs of disease; and the fourth, of the clinical applications of what has preceded in the diagnosis of the many different diseases. As a matter of fact the first three sections of the book (about 600 pages) comprise what would ordinarily be included in a handbook of diagnosis or of methods of diagnosis, while the last section (about 800 pages) is devoted to a discussion of subjects ordinarily included in a practice of medicine—definition, etiology, morbid anatomy, symptoms, diagnosis, and prognosis: treatment only is wanting.

Of the first part, one must say that it has been well done. The introductory remarks on diagnosis—direct and indirect—are extremely pertinent, and really should be read. The chapter on medical topography comprises a brief and satisfactory discussion of the topographical relations of the various landmarks of the body and the viscera, of value in all diagnostic procedures; and the chapter on case-taking includes all that is necessary to the subject. Of the subjects discussed in the second part, most interest undoubtedly attaches to physical diagnosis—inspection, palpation, mensuration, percussion, and auscultation—to which 133 pages are devoted. This in general is a reflection of recognized facts and opinions, tinged by the author's wide experience and ripe judgment. There is much that is excellent; for instance, the distinction drawn between loudness and accentuation of the heart sounds: loudness is said to be a matter of degree, accentuation a matter of quality, conveying the idea of suddenness, sharpness, and a certain vibrating

quality due to quick and sharp tension. Some of us, however, hardly dissociate entirely the element of loudness from accentuated heart sounds, as Dr. Wilson seems to imply. The apex of the heart is correctly said to be 2 to 3 cm. below and to the left of the maximum beat. It would have added to the interest of the discussion to have included an interpretation of sphygmograms in the light of our newer knowledge of cardiac physiology and pathology. Although it is true that a thrill at the base of the heart of maximum intensity in the aortic area is common in aortic stenosis, this thrill is systolic in time (which is not mentioned on page 94), and a systolic thrill in the same region occurs commonly in the absence of stenosis of the aortic orifice. Some confusion is likely to arise from the use, in regard to percussion, of the term "clear" for what is perhaps the more commonly employed term "resonant," and from a description of normal tympanitic areas in the chest; at the most these areas yield a note of mixed pulmonary resonance and tympany. "Suberepitant" applied to a rale is a really bad term and, although rather widely employed, should be discarded. The discussion of the methods of examining the stomach, intestines, upper air passages, blood, urine, sputum, transudates, exudates, the nervous system, and the eye are admirable. Attention might be directed to the absence of mention of the benzidine test for occult blood; and it would not have been amiss to have included some discussion of the methods of estimating the functional capacity of the heart, kidneys, etc. The diagnostic uses of the x-rays are well portrayed.

Part III, devoted to the symptoms and signs of disease, includes a discussion of the general appearance of the patient, temperament, and diathesis; the facies, weight, form and nutrition; the bones, joints, musculature, posture, attitude, and gait; the heat mechanism and fever; respiration, cough, and expectoration; the different types of pulsations; and the various manifestations of disease of the different systems of organs. Amidst a plethora of excellent matter it is difficult to pick out any one topic for special mention, but attention may well be drawn to the excellent discussion and analysis of pain. Part IV, is, as has been said, a modified practice of medicine—minus treatment. In general this is all that reasonably could be desired. The portrayal of the clinical aspects of disease and of their differentiation is clear and to the point; there are few omissions and still fewer misstatements. Mention should have been made of searching the urine for lead in cases of lead poisoning. Gallstones are still believed to rest quiescent in the gall-bladder in many cases without causing symptoms, although it has been well demonstrated that they frequently provoke divers sorts of "indigestion." On the contrary, Dr. Wilson well points out the fact that symptoms of gallstone colic are sometimes present in acute cholecystitis without gallstones; this is only part of the evidence that most cases of gallstone colic are really attacks of acute cholecystitis. The bad classification of chronic

interstitial hepatitis, or cirrhosis of the liver, depending upon the size of the liver, that is, upon whether it is of about normal size, atrophic, or hypertrophic, is adhered to, although as a matter of fact the size of the liver bears no constant or direct relation to the other phenomena of the disease. It is somewhat of a shock to be told that the right-sided hydrothorax of cardiac disease is probably due to the larger space in the left thorax occupied by the enlarged heart. The symptomatology and diagnosis of diseases of the blood and the ductless glands are very well described; but the characteristic remissions of pernicious anemia might have been more emphasized. There is no mention of the unusual cases of chronic adhesive pericarditis that run their course under the guise of cirrhosis of the liver with ascites; nor of Traube's sign in aortic insufficiency, nor is an explanation of the cause of the Flint murmur attempted. The murmur of mitral stenosis is correctly said to occupy the entire diastolic period in the greater number of cases. Much more might be said—mostly in praise of the volume.

Dr. Wilson set himself the task of encompassing within a single volume a description of clinical phenomena, and of correlating with these, complexes of clinical phenomena that constitute diseases, in such a manner that the practitioner who seeks information upon an obscure case may at once turn to the discussion of the methods available to clear it up, and the student may find the definite clinical applications of the same methods and their results in descriptive medicine. How well he has accomplished his task must be immediately apparent to any one who reads the book. If some of the foregoing remarks be construed as adverse criticism, one must hasten to add that they are minimal as contrasted with the general excellence; they are scarcely blemishes on a masterpiece. The book throughout reflects thoroughness and care in preparation; it is well arranged, lucidly written, and admirably illustrated; it is a credit to its author, and assuredly will meet, as it merits, a cordial reception on the part of the profession.

A. K.

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THIRD REPORT OF THE WELCOME RESEARCH LABORATORIES AT THE GORDON MEMORIAL COLLEGE, KARTOUM. By ANDREW BALFOUR, M.D., Director. Pp. 477; 266 illustrations. London: Baillière, Tindall & Cox, 1909.

THE director of the Wellcome Research Laboratories in Khartoum aims to issue a report at intervals of about every two years. This recently published third report leaves no doubt of the breadth and usefulness of the work which the laboratory has carried on. The subjects are so multiple that the book contains discussions in many of the biological sciences as they apply to the Sudan. The director



contributes a number of papers dealing with the protozoan diseases in man and in various domestic animals, and trypanosomiasis, hemogregarine, and spirochetosis of fowls are discussed. The subject of kala-azar as found in the upper Nile region is interestingly considered by other authors, special reference being made to the sanitary problems involved. The zoölogical papers concern, among other subjects, the reptiles and poisonous snakes of the Anglo-Egyptian Sudan. An extensive report by the economic entomologist is published, while several papers deal with characteristics of negroid tribes, ethnological specimens, and native medical practice in an interesting manner. The report of the chemical section deals largely with a research upon the native vegetable germs. The report contains and aims to disseminate much information of practical value to the people living in British African possessions, although many facts of purely scientific interest are also set forth. A noteworthy feature of the book is the illustration, consisting of colored plates, microphotographs, charts, maps, and photographs. The report reflects much credit on the director and the band of workers about him, who are making such strides toward bringing the Sudan into a higher state of civilization, and who are doing so much to elucidate the many problems in the natural sciences which abound in that country.

G. C. R.

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PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES, AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by HOBART ARMORY HARE, M.D., Professor of Therapeutics and Materia Medica in the Jefferson Medical College; Assisted by H. R. M. LANDIS, M.D., Demonstrator of Clinical Medicine in the Jefferson Medical College, Philadelphia. Vol. I, March, 1910; pp. 322; 8 illustrations. Philadelphia and New York: Lea and Febiger, 1910.

THE first volume of *Progressive Medicine* for 1910 opens with an instructive chapter of almost one hundred pages on the surgery of the head, neck, and thorax, by Charles H. Frazier. Special attention is devoted to trigeminal neuralgia, facial paralysis, brain tumors (including those of the hypophysis), papilloedema, hydrocephalus, cranial trauma, rhinoplasty, carcinoma of the lip, tongue, tonsils, and larynx, tuberculosis of the cervical lymph nodes, aberrant thyroids, goitre, tuberculosis and tumors of the mammary gland, empyema, pneumectomy with the aid of differential air pressure, the surgical treatment of pulmonary tuberculosis, wounds of the lung and of the heart, œsophagoscopy, and other important subjects. John Ruhräh has a chapter of eighty pages on the infectious diseases, in which he discusses especially the principles of the Wassermann

and similar reactions, the transmission of infectious diseases, pathogenic protozoa found in man, the treatment of acute infectious diseases with extracts of washed leukocytes (Hiss), vaccine therapy, cerebrospinal fever, "common colds," dengue, diphtheria, the "fourth" and the "fifth" disease, glanders, kala-azar, leprosy, malaria, measles, pneumonia, anterior poliomyelitis, rabies, Rocky Mountain spotted fever, scarlet fever, sleeping sickness, tuberculosis, typhoid fever, uncinariasis, pertussis, etc. Floyd M. Crandall devotes thirty-two pages to recent progress in diseases of children, discussing particularly infantile mortality, the care of the newborn infant, asphyxia neonatorum, septic infection and icterus in the newborn, the urine in infancy, status lymphaticus, rachitis, functional neuroses in children, infant foods, breast feeding, and artificial feeding. D. Braden Kyle devotes fifty-four pages to rhinology and laryngology, in which he treats especially of "taking cold," the treatment of chronic disease of the nose, recurrent nasal hemorrhages, hay fever, nasal tuberculosis, scleroma of the upper respiratory tract, sarcoma of the nose, the relation of the optic nerve to the nasal sinuses, suppuration of the accessory sinuses, pharyngoscopy, the faucial tonsils and the teeth, tonsillectomy, cicatricial stenosis of the larynx, laryngeal tuberculosis, voice production, phonasthenia in singers, etc. Arthur B. Duel devotes thirty-six pages to otology, treating especially of the labyrinth and its disorders, suppurative otitis, sinus thrombosis, syphilis in relation to the ear, and deaf mutism. The volume, as preceding volumes, merits the careful attention of all who would keep abreast of the progress of present-day medicine.

A. K.

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MEDICAL GYNECOLOGY. By SAMUEL WYLLIS BANDLER, M.D., Adjunct Professor of Diseases of Women, in the New York Postgraduate Medical School and Hospital. Second edition; pp. 698; 150 illustrations. Philadelphia and London: W. B. Saunders Company, 1909.

THE publication of a second edition within the year speaks well for the value of this work. As stated in the review of the first edition, in these columns, the book is a most complete exposition of non-operative gynecology. The present edition is a little larger than the earlier one, a matter of some twenty pages, due to the incorporation of new material, particularly in relation to the so-called Head zones, an instance of unfortunate nomenclature, together with several other and less extensive additions. It gives us pleasure to reiterate at this time the opinion formed by the critical review of the first edition, namely that the work is most satisfactory and that it will be found to be a valuable addition to the library of the general practitioner.

W. R. N.

A TEXTBOOK OF PRACTICAL THERAPEUTICS. By HOBART AMORY HARE, M.D., B.Sc., Professor of Therapeutics and Materia Medica in the Jefferson Medical College, Philadelphia. Thirteenth edition; pp. 958; 126 illustrations. Philadelphia and New York: Lea & Febiger, 1909.

The publication of a thirteenth edition of a book is in itself sufficient evidence of its unusual merit; and when to this is added the fact that a second Chinese edition has been published and that a Korean edition is about to be issued, the ever-widening sphere of influence of the book is immediately apparent. In the latest edition, Dr. Hare has, as he has heretofore, thoroughly revised his *Therapeutics*, so as to have it fully abreast of the times and make it adequately meet the requirements of the general practitioner. Among the inclusions, one may mention, the use of atoxyl as a substitute for the older arsenical preparations, and especially its use in syphilis; phenolphthalein in constipation; salicylate of ethyl and novaspirin in rheumatic and gouty affections and aspirin locally in tonsillitis; magnesium sulphate locally for the relief of pain and inflammation; picric acid in burns; urotropin to prevent cholecystitis in typhoid fever and infection after injury of the cerebrospinal system; the Lenhartz method of treating gastric ulcer; Murphy's method of treating septic peritonitis; antitoxins for gonorrheal infections and cerebrospinal meningitis; and recent researches on anesthetics. The book thus comprises not only a discussion of materia medica, and of the properties and actions of drugs and other remedial measures, but also describes the practical applications of these measures to the every-day treatment of disease. There is perhaps no more popular book, and none more deservedly so. In its new edition it will unquestionably maintain the enviable position that it has achieved, and it must also command an ever increasing circle of professional adherents.

A. K.

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A TEXT-BOOK OF OBSTETRICS. By BARTON COOKE HIRST, M.D., Professor of Obstetrics in the University of Pennsylvania. Sixth edition; pp. 992; 847 illustrations. Philadelphia and London: W. B. Saunders Company, 1909.

ONE of the developmental changes in medical work, destined before long to become a matter of common acceptance by the profession and the public, and even now beginning to be appreciated, is that obstetrics is a branch of surgery. The ordinary obstetric case should have for its safe conduct a degree of asepsis not less than is demanded by other procedures recognized to be within the domain of surgery, while operative obstetrics is of course admittedly surgical.

The truth of the foregoing being self-evident, it naturally follows that a man competent to handle ordinary obstetric complications will be expected, and must without question be prepared, to treat the consequent lesions or the complications of the child-bearing process. In other words, the obstetrician of the present and future must be a skilled gynecologist. In his preface to this, the sixth edition of his work, the author emphasizes the essential connection between these two subjects, and calls attention to the futility of advising various needful operative procedures in obstetric text-books without advice as to the necessary technique of their performance. He has, therefore, in the present edition included in his section on operative obstetrics a full consideration not only of the so-called obstetric operations, in the usually accepted narrow meaning, but also those operative procedures commonly classed under the artificial limitations of gynecology.

The previous editions of this work have made its character and scope so well known that it seems unnecessary to review it again in these pages in extenso. The wide experience of the author as a teacher and operator has enabled him to produce a book which, in scope and detail, is not surpassed by any other yet published upon this subject.

W. R. N.

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ORGANIC AND FUNCTIONAL NERVOUS DISEASES. By M. ALLEN STARR, M.D., Ph.D., LL.D., Sc.D., Professor of Neurology in the College of Physicians and Surgeons, Columbia University, New York. Third edition; pp. 911; 329 illustrations. Philadelphia and New York: Lea & Febiger, 1909.

But two years have elapsed since the publication of the second edition of Dr. Starr's well known book of *Organic and Functional Nervous Diseases*, and a demand is made for a third: certain evidence of intrinsic worth and merit. The opportunity was embraced to revise, and rearrange the contents and to make many additions. The general aspects of neurology, including anatomical and physiological details, the method of examining a patient, the various symptoms presented by nervous affections, and the principles of diagnosis, have been brought together in the first part. The organic diseases are discussed in the second part; such additions as have been made to our knowledge of the nervous system since the publication of the second edition have been incorporated; and the chapters on beri-beri, caisson disease, and syphilis have been rewritten. The functional nervous diseases are discussed in the third part—which has been about doubled in size. In the fourth part the diseases of the sympathetic nervous system are discussed, our present knowledge of vasomotor affections, their physiology and pathology being sum-

marized, and chapters added on symmetrical gangrene, angioneurotic œdema, and the trophic symptoms occurring in nervous disorders. The indications for surgical intervention in many disorders of the nervous system and the operative procedures to be elected are fully set forth, all of which is based upon a large personal experience as well as judicial sifting of the writings and experience of others. The book assuredly is of much value and a credit to its author; it must continue to enjoy the favor of the profession. A. K.

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THE INTERPRETATION OF RADIUM. By FREDERICK SODDY. M.A. of the University of Glasgow. Pp. 256; 31 illustrations. New York and London: Putnam, 1909.

THIS book aims at a presentation of the present-day views of radium, as an element undergoing spontaneous disintegration. Non-technical language is used, so that the ideas involved may be comprehended by the lay reader. Beginning with a description of radioactivity and its effects, the history of the discovery of radium and the development of our knowledge of its properties are considered in logical order to the latest view that lead is the end product of a series of changes which begins in the element uranium. Briefly, each of these changes consists of the giving off of an atom of helium from an atom of uranium or one of the resultants, each change reducing the element to the next lower in the series. Uranium has an atomic weight of 238, and lead 206, the difference between them representing eight atoms of helium given off at eight different periods of disintegration. This process constitutes a veritable transmutation of elements. The subject deals in measurements so enormously large and so infinitely small that it taxes the imagination of the reader to comprehend it. For instance, the "average life" of uranium is 7,500,000,000 years, and "a grain of radium bromide expels every second about ten thousand million particles throughout many centuries." One pound of uranium contains latent energy equal to that of 900 tons of coal, etc. The application of radium to medicine is not discussed, but the last chapter is devoted to speculation as to the results to the human race of future generations of the possible utilization of the enormous energy stored in matter. Taken as a whole, the work is clear and convincing, and the illustrations are of material aid to an undertsanding of the methods employed in investigating this subject. S. D. I.

# PROGRESS OF MEDICAL SCIENCE.

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## MEDICINE.

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UNDER THE CHARGE OF

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**Blood Findings in Pulmonary Tuberculosis.**—STEFFEN (*Deut. Arch. f. klin. Med.*, 1910, xeviii, 355) has made a careful examination of the blood of 79 tuberculous individuals (sanitarium patients). In all instances the blood was obtained between the hours of 6 and 7 A.M. Differential counts were made of specimens stained with Leishman's stain, 1000 cells being counted as a rule. The chief interest centres in Steffen's findings with regard to the lymphocytes and polymorphonuclear neutrophiles. In chronic afebrile cases the polymorphonuclear neutrophils are normal (absolute number), and lymphocytes are about doubled in number. In acute defervescing cases, the polymorphonuclear neutrophils are normal or slightly diminished, whereas lymphocytes are two to three times the normal number. In the severe (advanced) cases there is an increase of the polymorphonuclear neutrophils. Cases of moderate severity show, as a rule, an absolute increase of both polymorphonuclear neutrophils and lymphocytes. Steffen believes that the lymphocytosis is to be attributed to the tuberculous process *per se*. As soon as the infection becomes mixed, with ulceration and caseation, a polymorphonuclear neutrophil increase may be expected, its extent being governed by the same factors which are operative in any pyogenic process. The lymphocytosis which occurs early is of considerable diagnostic value. True, such a finding may occur in lues, Basedow's disease, whooping-cough, nephritis, etc., but the finding of an abnormally large number of lymphocytes should awaken one's suspicions, and in the presence of other signs it is confirmatory evidence. Lymphocytosis may occur before bacilli are demonstrable in the sputum. In an outspoken case of pulmonary tuberculosis

losis, the author believes one may draw definite conclusions as to the nature of the pulmonary process—whether tuberculous alone or secondarily infected—from the differential count, and, in a general way, as to the predominance of one or the other factor.

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**Determination of Urinary Ammonia and Acidity.**—BJORN-ANDERSON and FAURITZEN (*Hoppe-Seiler's Zeit. f. physiol. Chem.*, 1910, lxiv, 21) describe a simple and rapid method for determining urinary ammonia and acidity. Comparative tests show that the  $\text{NH}_3$  values are constantly a little too high. The principle of the method is as follows: We have, let us say, one fluid which contains  $n$  equivalents of an acid— $\text{HCl}$ , for example—and  $m$  equivalents of an ammonium salt, such as  $\text{NH}_4\text{Cl}$ . Since the latter is neutral in reaction,  $n$  alkali equivalents will be necessary to neutralize the fluid. If formalin (40 per cent. formaldehyde) be added to a fresh portion of the fluid, it unites with the  $\text{NH}_3$  of the ammonium salt to form hexamethylenetetramin, and hydrochloric acid is set free. On titrating now, it will require  $n + m$  alkali equivalent to neutralize ( $n$  for the original acid present and  $m$  for the acid set free by the formalin). By subtracting the first value (cubic centimeter of  $\text{N}/10$  alkali) from the second, one obtains the number of acid equivalents which were bound by  $\text{NH}_3$ . The quantity of ammonia in grams is obtained by multiplying by 17. Before titrating, the fluid should be saturated with neutral potassium oxalate, as Folin has shown, to remove the calcium. Method of titration: To 20 c.c. urine add 20 grams of finely powdered neutral potassium oxalate and 5 drops of 0.5 per cent. solution of phenolphthalein. Now add  $\text{N}/10$   $\text{NaOH}$  to neutralization. The number of cubic centimeters required is noted and then 5 c.c. formalin (neutralized, if necessary) is added. Again add decinormal alkali sufficient to neutralize. The quantity of alkali used in the last titration indicates the amount of acid which was bound by ammonia. The fact that the readings are somewhat high is probably due to the presence of amino-acids in the urine, since formaldehyde unites with the amino group and liberates the acid radicles. In following the urinary acidity and ammonia in diabetic acidosis during the last three years, it has been found that the method gives satisfactory results. It has been noted that the ammonia and acidity curves run a parallel course. This parallelism has been seen in health as well as in diabetics and, apparently, has not been previously observed. It shows that one can follow the variations in the degree of acidosis by determining the total acidity of the urine. In recent years there has been much discussion as to whether the absolute amount of  $\text{NH}_3$  or the ratio of  $\text{NH}_3$  nitrogen to total nitrogen is of greater value in determining the grade of acidosis. Bjorn-Anderson and Fauritzen believe that the absolute amount of  $\text{NH}_3$  is the more important.

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**Experimental Acute Nephritis.**—PEARCE, HILL, and EISENBERG (*Jour. Exper. Med.*, 1910, xii, 197) have continued on dogs the experimental work done by Sehlager and his associates on rabbits. Their studies have been especially directed to the vascular reactions which are present in the tubular and vascular types of nephritis. Potassium chromate, uranium nitrate, and corrosive sublimate produce lesions

which are, in the early stages, of a nearly pure tubular type, while arsenic and cantharidin cause directly vascular disturbances. Late tubular nephritis is of a more mixed type. The vascular reactions of the kidney were determined by measuring with an oncometer the changes in the volume of the organ occurring under the influence of adrenalín to cause contraction of the vessels, and of caffeine and sodium chloride to test dilatation and diuresis. In the early cases of tubular nephritis the animals usually present an initial polyuria; the vascular reactions are normal or exaggerated, and with increased dilatation due to the administration of caffeine and salt solution, there occurs a correspondingly greater diuresis. While these cases show no anatomical lesions in the glomeruli, the exaggerated vascular reactions and increased diuresis point to a functional disturbance of the vessels, presumably an increased excitability. The vascular poisons, arsenic and cantharidin, on the other hand, produce little injury to the epithelium, but tend to cause anuria, and are characterized by minimal contraction and dilatation of the vessels, and little or no flow of urine. The late cases of tubular nephritis may be divided into two groups: One, the anuric form, is accompanied by severe gastro-intestinal disturbance and evidence of approaching anuria; physiological tests show diminished power of dilatation of the vessels, and corresponding inhibition of diuresis. The second form, the polyuric, is characterized by a condition of polyuria up to the moment of anesthesia. Physiological tests show that the power of dilatation is retained, but little or no diuresis occurs. The vascular incompetency in the late stages of the anuric form of tubular nephritis may be a natural consequence of the vessel irritability seen in the early stages, or it may be due to the elimination of secondary poisons through the glomeruli. The impermeability of the glomerulus following anesthetization in the polyuric form is as yet unexplained. Studies of the elimination of nitrogen were carried on in the same experiments. In tubular nephritis, especially the type produced by uranium, the output of nitrogen is diminished, and with its retention gastro-intestinal disturbances appear. There is, however, no appreciable change in the amount of nitrogen in the feces, so that the intestinal symptoms do not depend on the elimination of toxic bodies of nitrogenous nature through the intestine. In the vascular nephritis caused by arsenic, the nitrogen elimination is increased owing to the increased metabolism caused by arsenic. It may be markedly diminished, however, by the administration of uranium nitrate. The general results obtained incline the authors to conclude that while it is not possible to demonstrate that an experimental nephritis may be purely tubular or purely vascular, lesions may be recognized which are predominantly of one type or the other, or which change rather sharply from one to the other type, and are, therefore, of great value in the study of problems of nephritis.

**The Effect of Serum Injections on the Eosinophiles and Mastzellen in Man and Animals.**—SCHLECHT (*Deut. Arch. f. klin. Med.*, 1910, xcvi, 308) reports interesting changes in the leukocytic formula following injections of antidiphtheritic and other sera. In diphtheria in man, when untreated with antitoxic serum, there is an initial leukocytosis of the polymorphonuclear neutrophile type, other cells showing no increase, eosinophiles and mastzellen often disappearing. While the



febrile reaction persists, the neutrophiles gradually diminish and there is a more or less marked reparatory increase of the large mononuclears. With defervescence there is a lymphocytosis, and coincidentally the eosinophiles and mastzellen reappear and may even be more numerous than normally. When antidiphtheritic serum is given, the blood picture is altered. Within twenty-four hours after the first serum injection, an eosinophilia often appears and persists into convalescence. This amounted to 18 per cent. in one case (10,000 white blood corpuscles per 1 cm.); in another 14 per cent. of 13,000 leukocytes. Schlecht resorted to animal experiments to determine whether the eosinophilia resulted from the antitoxin, the serum, or the carbolic acid used as a preservative. Young guinea-pigs were used. Schlecht's observations on man and animals led to the following results: (1) Eosinophilia may be produced in man by the injection of antidiphtheritic serum; as a rule, children react more rapidly and oftener than adults. The reaction has no prognostic value. (2) Animal experiment shows that the reaction is not specific for antidiphtheritic serum, but that it may follow the injection of any foreign serum. (3) Usually there is an initial drop in the number of leukocytes with hypo-eosinophilia; an increase in the white count and hypercosinophilia quickly ensue. (4) In addition to eosinophilia, guinea-pigs show a great increase in the number of mastzellen following the injection of serum, the two appearing together or independently. (5) No increase of mastzellen occurs in man or the dog. The cause of the reactions is found in functional hyperactivity of the bone marrow.

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## S U R G E R Y.

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UNDER THE CHARGE OF

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**Intravenous Narcosis.**—KUETNER (*Zentralbl. f. Chir.*, 1910, xxxvii, 233), having employed this method of narcosis in one case unsuited for inhalation or local anesthesia, and being impressed by its success and apparent lack of danger, enlarged its use and now has employed it in 23 cases. He does not recommend it, however, but warns against it. In spite of all care and the exact observance of Burkhardt's precautions, thrombosis can occur at the site of the infusion even during the anesthesia. In two cases the saline infusion containing the ether failed to flow into the vein, and it was necessary to expose a second vein. During the operation on one case, the removal of a sarcoma in the gluteal region

involving the pelvis, the patient suddenly became cyanotic, the blood dark and the breathing shallow and rapid. The pulse, however, remained good and the pupils reacted. The infusion was stopped immediately, and the normal condition soon returned. Investigation showed that the vein was completely closed by a recent thrombus, the size of a pea. The transitory disturbance was probably due to an embolus. On the following day there was much disturbance in breathing, although the general condition was good. In another case in which there was no disturbance at the time of operation, on the day following operation, an extensive infiltration of the right lung was found and there was fever. The method, nevertheless, has advantages for the patient and the operator, especially in extensive operations about head and neck; and it is hoped that improvement in it may avoid its present dangers.

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**The Technique of Hemostasis in Operations on the Skull.**—VORSCHUETZ (*Zentrbl. f. Chir.*, 1910, xxxvii, 274) provides hemostasis in the central flap by the use of a needle passed from one side to the other, under the base of the flap between the periosteum and bone, 1 cm. below the end of the flap. There is an outer band with a hinge at one end and a spring catch at the other, which encloses the end of the needle and provides compression of the bloodvessels entering the flap. When the flap is outlined by the incision, the peripheral edge of the incision is compressed by a series of hemostatic clamps with wide jaws, the handles of the clamps being directed away from the wound and lying in contact with the surrounding scalp out of the way. The advantages of the method are: the rapidity with which the edges are caught; retractors are unnecessary, since the clamps are used for this purpose; the clamps are so shaped and directed that they are not in the operator's way; the skin is not pulled out of place so that the topographical lines on the surrounding skin are not distorted. The skin sutures for closing the wound should be close together, about 0.5 to 1 cm. apart, and if a vessel spurts it should be enclosed in the suture.

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**Studies on the Infusion of Physiological Saline Solution.**—THIES (*Mitt. a. d. Grenz. d. Med. u. Chir.*, 1910, xxi, 239) says that the physiological (9 per cent.) or the pure saline solution is not entirely suitable for infusion in the sick. They may, under certain circumstances, lead to severe disturbances and are to be avoided, especially, in small children, in patients who have lost much salt in conditions of hunger, in cachexia, and in patients who have associated pathological conditions of the kidneys, heart, and vascular system. It is not to be employed in those in whom there is a retention of sodium chloride, or an increased secretion of other salts, and is to be avoided in all fever patients. It is likewise to be excluded in cholemia, and should not be employed when large quantities of saline solution are required. The danger to the body is the greater, the greater the substitution of the alkaline substances of the cells for the sodium, which alters unfavorably the normal relations in the cell protoplasm. Since potassium and calcium are important metals for the preservation of life and function, it is necessary to prevent crowding them out of their relative positions by the presence of the sodium in the saline solution. Potassium and calcium should be added

to the sodium chloride in the solution, about in the proportion in which they occur in the body, that is, sodium chloride about 0.6 per cent., calcium chloride about 0.02 per cent., and potassium chloride about 0.02 per cent. This solution is hypotonic in relation to the serum, yet the injury which may result from this is less than that which would result from a pure sodium chloride solution. If the solution is to be isotonic to the serum, as is desirable in subcutaneous infusions, then not only the sodium chloride but the potassium and calcium salts also should be increased, so that the following proportions are present: sodium chloride 0.85 per cent., potassium chloride 0.03 per cent., and calcium chloride 0.03 per cent.

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**The Treatment of Hydrocephalus with Repeated Puncture.**—KAUSCH (*Mitt. a. d. Grenz. d. Med. u. Chir.*, 1910, xxi, 300) says that in hydrocephalus in children, when the skull is wide open, the ventricular puncture should be made through the opening in the skull. The degree of pressure should be determined at the beginning and ending of the puncture. At the first puncture in severe cases, about 100 cm. should be withdrawn. The increased pressure should sink, about 20 cm. of water, but not lower than + 5 cm. If the child bears this well, at the next puncture the pressure should be brought down to 0, and later to minus. The quantity evacuated each time can be increased gradually to 200 or 300 cm. The puncture should be repeated as soon as a higher positive pressure is suspected, if necessary daily, otherwise every few days, until the skull reaches the normal size. When there is a negative pressure and especially if the bones remain separated after the evacuation, compression should be employed. Lumbar puncture is to be employed, if the skull is open, only in mild cases, or in severe cases when a considerable improvement has followed ventricular puncture, and the removal of a greater quantity cannot be undertaken. The more advanced the closure of the skull, so much more careful should one be, especially with associated negative pressure. One must proceed very carefully in closed skulls, in order to avoid completely negative pressure or a marked decrease of increased pressure, at one sitting. One should desist frequently and every time withdraw less. Then the lumbar puncture should be employed. If this is not successful, repeated ventricular punctures should be made through a small trephine opening, best in the frontal region. The complicated methods of operation should not be attempted in an open or closed skull until repeated and energetic punctures have been tried and have failed to accomplish their purpose.

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**Six Cases of Hypogastric Retrograde Catheterization.**—HACHE (*Ann. d. mal. a. org. gen-urin.*, 1910, 1, 233) did retrograde catheterization in six cases. In the first case there was an old fracture of the pelvis, with a splinter of the pubis situated along the urethra between two strictures. An external urethrotomy was performed, a hypogastric incision becoming necessary for retrograde catheterization. An internal urethrotomy was also necessary. In the second case urinary extravasation resulted from an old stricture, with an impacted calculus in the urethra. Besides the hypogastric catheterization an internal urethrotomy was performed. In the third case there was a fracture

of the pelvis with a laceration of the prostatic urethra and a tear of the rectum. Infiltration of urine resulted, calling for an external urethrotomy and retrograde catheterization. In the fourth patient an insuperable gonorrhoeal stricture called for retrograde catheterization and an internal urethrotomy, and in the fifth, in which the same condition was present and the same treatment carried out, the union in the bladder and urethral wounds was immediate and the stricture rapidly recurred. In the sixth case, a tight stricture was treated first by internal urethrotomy, then by external urethrotomy, and forty-five days later a hypogastric retrograde catheterization was necessary. He emphasizes the absurdity of the diagnosis of a foreign body in the urethra in connection with the first case owing to the few symptoms present; the difficulty one may experience in opening the empty bladder for retrograde catheterization; and the repair of the urethra after trauma or operation. The method of finding the urethra through the perineum posterior to the lesion, at the apex of the prostate, is more inconvenient and laborious than by the hypogastric and bladder route.

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**The Treatment of Dry Arthritis with Injections of Vaseline.**—ROVSING (*Annals of Surgery*, 1909, 1, 1052) has injected 53 joints with vaseline, but bases his conclusions on the results of 35 of these in 30 patients. He has been able to control the results at least eighteen months. These cases he divides into two main groups, of which the first, consisting of 7 cases, comprises the non-traumatic "dry" arthritis, is of rheumatic, uratic or unknown origin; while the last group comprises the traumatic dry arthritis, into which comes the senile disorder, together with 4 cases in which vaseline has been injected in order to prevent ankylosis after arthrotomy and arthrectomy—23 in all. The result of his experiments with the injection of vaseline in the cases of really chronic apparently dry arthritis of uratic, rheumatic, or other infectious origin was as follows: If by the puncture fluid is found in the joint, one ought to abstain from the vaseline treatment completely; if, however, the joint is found completely dry and the inflammation apparently extinct, one ought to attempt the injection of a smaller quantity of vaseline, which cannot distend or strain the capsule, afterward watching any possible return of the symptoms of inflammation. In two of the non-traumatic cases, finally, a good functional result was obtained. In the traumatic cases the results were almost constantly satisfactory. The injection should be made under absolutely aseptic precautions, and the quantity injected should vary with the size of the joint. Considerable experimentation was necessary in deciding for each joint the necessary quantity. In adults the hip will take without difficulty, 20 to 25 c.c; the knee, 10 to 12, and 15 at the most; and in the shoulder, 15 c.c. will be suitable, as a rule.

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**Principles of a Radical Treatment for Proctosigmoiditis.**—BASTIANELLI (*Annals of Surgery*, 1909, 1095) has in recent years, seen a relatively large number of these cases, commonly called strictures of the rectum, but which really involved greater problems than those connected with a simple stricture. Prominent among the anatomical conditions to be considered in the treatment is not the stricture itself but the inflamma-

tion of the rectum and its extent, since the stricture is a limited consequence only, not the essential disease; so that if we succeeded in removing only the strictured part we have done nothing at all in the majority of cases, the inflammation being still there with all its actual symptoms and promise of a new stricture in the future. An exploratory laparotomy is necessary for examination of the intestine as a preliminary to the radical treatment. This will permit the establishment of an artificial anus, which will give the inflamed parts a long period of rest, and thus the patient an opportunity to recuperate from his poorly nourished, emaciated, and often, cachectic condition. The artificial anus is also a safety valve allowing aseptic operating and a clean after treatment. The radical operation will now follow, and it will be guided by what the preliminary exploration has ascertained. If the lesion is a limited one, a perineal extirpation may be performed; if extensive, resort must be had to a combined abdominal and perineal operation, in both cases the aim being to preserve the function of the sphincter and to put into it a healthy portion of bowel. In stricturing proctitis or proctosigmoiditis, therefore, the treatment should be: (1) Cecal anus and laparotomic exploration of the bowel. (2) Perineal or combined removal of the diseased section in one or two stages, with mobilization of the sigmoid and colon if necessary, and preservation of sphincter. (3) Closure of the cecal anus. (4) Plastic operation if necessary. Bastianelli emphasizes the importance of resorting more frequently to the abdominal route in the treatment of stricture of the rectum for the purpose of preliminary exploration, and the importance of exact ligating and cutting the arterial supply from the abdomen, even in cases of perineal operation, to prevent any damage to the circulation.

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**Intestinal Obstruction in Children.**—ALAPY (*Archiv. f. klin. Chir.* 1910, xel, 803) reports the results of his observations on 45 personally observed cases of intestinal obstruction in children. The ages of the patients varied from that of a nursing infant to fourteen years. Intestinal obstruction is more readily recognized in children than in adults. In children, it is generally due to two pathological conditions, appendicitis and invagination. In Alapy's 45 cases, there were only 5 which were not due to one or the other. Those due to appendicitis were observed in ten different forms; dynamic ileus of acute inflammation, adhesive ileus of acute inflammation, strangulation after the disappearance of the acute stage, early form of postoperative adhesion ileus, late form of the same, occlusion from progressive peritonitis, from abscess in Douglas' pouch, reflex (spastic) obstruction, obstruction from a strangulated or inflamed appendix in a hernial sac, and ileus in consequence of a diffused peritonitis. On the other hand, the invagination group were uniform. Whether the cause was the same or different, the clinical picture was nearly the same. It is best not to concern oneself with an unsatisfactory classification. From case to case an effort should be made to establish an exact diagnosis concerning two points; (a) the pathological process involved, and (b) the site of the obstruction (not the portion of intestine involved but of the abdomen). One of the most important features is the presence or absence of tension of the abdominal wall. The absence

of this sign in all of Alapy's cases of invagination was of the greatest diagnostic importance in the differentiation from appendicitis. The treatment of intestinal obstruction in children differs in certain respects from that in adults. A rapid and sparing operation is often necessary to save life. Selfevidently, it must be applied to the pathological process present. Under similar circumstances, enterostomy has a wider range of usefulness than in adults. This is not merely a palliative operation. With two exceptions all the children who survived enterostomy, were radically cured. The effort to cure should be made not through resection but through disinvagination. Resection is only exceptionally necessary, and should be done only after disinvagination has been accomplished. The very frequent assertions that the attempts to disinvaginate fail because of the presence of adhesions, are based upon error. The cause of the failure is not adhesions, but a faulty technique. Alapy succeeded in disinvaginating all cases of ileocecal invagination. Firm adhesions were practically never present. The method of disinvagination was as follows: The anal end of the intestinal tumor is grasped in the fist and squeezed without shifting the hand from its place. If the oral end is kept in view, a small portion of the invagination at the neck can be seen emerging. The hand should now grasp a higher portion, again at the anal end of the mass, and the procedure should be repeated until the disinvagination is completed. In many forms of intestinal obstruction, an attempt at non-operative reduction is justified, provided the obstruction has not lasted long. It must be overcome quickly. The resistance of the child is less than that of the adult. Delay of operation is fatal. If a brief trial with non-operative reduction fails, operation should be done immediately.

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## THERAPEUTICS.

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UNDER THE CHARGE OF

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**General Principles of Tuberculin Diagnosis and Treatment.**—BALDWIN (*Jour. Amer. Med. Assoc.*, 1910, liv, 260) says that the therapeutic use of tuberculin may have two fairly definite objects in view: One is to diminish the sensitiveness to the toxin—that is, to itself; the other is to cause intermittent local reactions, and thus to stimulate the disease focus to heal or become absorbed. The possibility of the production of a recognizable immunity to the disease thus far by any form of tuberculin treatment is open to question. A certain degree of resistance is indirectly accomplished when sensitiveness to tuberculin is decreased to a marked degree, accompanied by constitutional improvement. The degree of tolerance or immunity to tuberculin is proportionate to the dose that can be borne without reaction. Hence the progressive increase of dosage

is essential. When only reactions about the focus of disease are desired the dosage need not be increased so long as sensitiveness persists to small doses. As soon as this sensitiveness is overcome the treatment should be interrupted until sensitiveness returns, or the doses must be increased to an unwise degree. Baldwin says that only patients in a quiescent state of the disease are likely to be benefited. Pulmonary patients should be in a good nutritive condition and free from persistent fever over  $100^{\circ}$ , hemoptyses, night sweats, chronic diarrhoea, or extensive laryngeal complications. The physical signs in the lungs should indicate a localized disease, free from large pneumonic consolidation or disseminated disease. Progressive tuberculosis of any form is a contraindication to this treatment. Reactions are to be avoided, and may involve danger when repeated, except in cases of well-arrested localized disease. Slight unperceived focal reactions probably occur under any plan of tuberculin treatment, and, when rightly timed, are beneficial. The author points out the obvious fact that focal reactions can be best observed and applied with safety in those cases of skin, bone, joint, or genito-urinary tuberculosis in which the lung is not involved. With reference to the choice of tuberculin, Baldwin says that opinions are too variant to permit the formulation of rules. In general the dosage is more controllable with solutions, and reactions are less frequent from emulsions. However, the absorption of emulsions is very uncertain, and reactions may occur unexpectedly with the increase in dosage. Therefore he believes that the solutions are safer for tuberculin immunization. The dosage is empirical and entirely dependent upon the individual case. The clinical symptoms are the most satisfactory guides, though opsonic determinations may be of value in the hands of experts. For the majority, the opsonic index is impracticable and misleading. Tuberculin should be administered subcutaneously. Tuberculin when given by the mouth or rectum is too uncertain of absorption to warrant any recommendation. Baldwin concludes by saying that the technique of tuberculin injections, the guide to correct dosage and intervals, are details which vary with the preparation used and the experience of different observers.

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**Total Energy Requirement in Diabetes Mellitus.**—DU BOIS and VEEDER, (*Arch. Int. Med.*, 1910, v, 37), upon the basis of a series of careful experiments, believe that the total energy requirement of diabetes does not vary so markedly from the normal as some other observers have maintained. They state that, in addition to the 31 to 35 calories per kilo required for the normal individual, only enough extra calories should be given to the diabetic to cover the loss of sugar in the urine. If this is not done the body protein and fat are broken down to supply the needed amount.

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**The Dietetic Treatment of Diabetes Insipidus.**—SCHÜTZ (*Berl. klin. Woch.*, 1909, xlviii, 2168) reports a case of diabetes insipidus treated with a salt-poor diet. The patient had lost thirty-five pounds, and that was his chief symptom. The daily amount of water ingested was at times over 40 liters. Before treatment the daily amount of urine was from 18 to 20 liters, with a specific gravity of from 1000.5 to 1001, with a sodium chloride content of from 32 to 34 grams and a total nitrogen of

from 22 to 23 grams. All mineral waters were forbidden and a salt-poor diet with a minimum of protein was ordered. The daily quantity of urine fell to from 6 to 8 liters daily, with a specific gravity of from 1002 to 1003. The sodium chloride content fell to 12.9, and coincidentally there was a great improvement as regards thirst. During six months the patient gained twenty-six pounds, with a marked improvement in the general condition.

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**Treatment of Diabetes Insipidus.**—MINKOWSKI (*Therapie d. Gegenwart*, 1910, i, 4) says that the daily amount of the urine in diabetes insipidus is at times dependent upon the amount of sodium chloride in the food. He advises the determination of the chloride content and specific gravity of the urine after the ingestion of a considerable amount of salt. If the specific gravity and chloride content increase relatively more than the amount of the urine, the power of concentration is still retained. Such cases are benefited by a restriction of the amount of fluids. On the other hand, if the dose of salt influences the amount of urine more than the chloride content, a diminution of the sodium chloride and the nitrogen in the diet is indicated. If no benefit results from the withdrawal of salt, Minkowski believes that the trouble is then probably due to some organic lesion of the nervous system. On the assumption that such organic disease is the result of syphilis, antisyphilitic treatment may prove of value.

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**Notes Respecting the Dietary of Goutily Disposed Persons.**—DUCKWORTH (*Pract.*, 1909, i, 1) says that in the treatment of gout the mistake is often made of treating according to system and of not considering the individual case. He believes, for instance, that there is no rule applicable to all gouty persons with reference to their allowance of meat. In general, meat in moderation is in no way harmful, but beneficial. Strong meat soups and beef extracts are to be avoided; pickled or salt meats are, as a rule, inadvisable, but they need not be absolutely excluded from the diet. He believes that meat should be roasted or broiled, that mutton is better than beef and much better than poultry for the average case. Liver, sweetbreads, and kidney should not be allowed. A purin-free diet works very well in many cases of gout. However, there are patients who cannot bear this diet long. Fish and some shell fish, if eaten fresh, are considered by Duckworth to be harmless. He allows ordinary bread, plain or toasted, or plain biscuits. He believes that plainly cooked potatoes are entirely harmless. Green vegetables, especially spinach, cress, and lettuce are of value. Asparagus should be given very sparingly. Fruits, both cooked and raw, may be given to gouty patients. Tea, coffee, and cocoa have no bad effects, with the exception of strong black coffee taken after meals, which he prohibits. A single wine in small quantity, preferably port, Bordeaux, or champagne, is allowed. He especially forbids large mixed meals of animal and farinaceous food elaborately prepared and richly seasoned. He forbids cooked tomatoes, rhubarb, and food cooked with fat or sugar. Sauces, relishes, and highly spiced food must be avoided. He believes that both lemon juice and vinegar are harmful. Mustard and salt may be taken in moderation. Abundant water should be given to gouty patients, and should contain little calcium or iron. He says that the continued use



of alkaline or lithia drinks often is harmful and should be forbidden. In general, Duckworth lays more stress upon the quantity of the food and the manner of its preparation, which should be simple, than upon a strict limitation of its character.

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**Flatulence and its Treatment.**—BOAS (*Berlin. klin. Woch.*, 1910, iii, 89) divides flatulence into several varieties, with corresponding differences in its treatment. One form, which he denotes as exogenous, is due to intake of gas while eating, and is usually observed in rapid eaters. A second form, associated with colicky pain and which he denotes as endogenous, occurs as a result of chronic constipation or inflammatory conditions of the small and large intestines. In this class may also be included the flatulence resulting from organic or less often functional spasmodic stricture of the intestine. Finally, passive congestion often is the cause of intestinal flatulence. Boas deprecates the treatment of flatulence by carminatives, and advises a rational treatment dependent upon the etiology. For the treatment of flatulence of alimentary origin, especially when associated with chronic constipation and catarrhal inflammation, the most important factor in the treatment is the exclusion of fermentable foods from the diet. Since individuals differ markedly with respect to their digestion of different foods, their tolerance for various foods must first be determined. Boas mentions milk, buttermilk, eggs, and rare meats among the foods most apt to result in fermentation. He lays particular stress upon the avoidance of raw or rare meats. Potatoes are also responsible for flatulence in individual cases. He considers magnesium salicylate, in doses of from 1 to 2 grams three times a day, the best antifermentative drug, and he says that it has the further advantage of not causing constipation. Boas advises small repeated doses of castor oil when constipation is associated with the flatulence. Surgical treatment alone is of value in the treatment of flatulence due to organic stricture. When the flatulence is due to passive congestion, cardiac tonics and diuretics are indicated.

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## PEDIATRICS.

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UNDER THE CHARGE OF

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**The Regulation of Fat Percentages in Infant Feeding.**—A. S. BLEYER (*Archives of Pediatrics*, 1910, xxvii) has made observations of the feeding in 600 infants, with special attention to the fats. He found that when the fats were reduced to less than 1 per cent. the child became very hungry, regardless of a reasonable increase of proteins. This effect was noticed whenever it was tried. The effect of fat-free feeding on the intervals of feeding, shows that a normal child will be hungry in about an hour and a half, and that the number of feedings depend in

great measure on the percentage of fat in the mixture. From a study of the influence of fats on vomiting, Bleyer concludes that the caseins offer little difficulty in vomiting in babies, if the fats do not interfere, and that the teaching on the formation and indigestibility of casein curds has been incorrect. A series of vomiting babies was selected in which sodium citrate had controlled the vomiting. The fats were then removed from the feedings and the sodium citrate discontinued. In the majority of cases the vomiting did not recur. He, therefore, concluded that a rapid precipitation of caseins did not often cause vomiting in the absence of fats. Again, if whole milk is precipitated, over 60 per cent. of the curd by bulk is fat. Furthermore, the curd is tough, leathery, and tenacious, which characteristics are never found in a simple casein curd without fat.

On the influence of fats on the character of the stools and on constipation, he reports 28 records kept of babies fed on a low fat percentage, in 20 of which there was at least one stool every day and a number had diarrhoea. Aside from these records, he has observed usually two or more stools a day in children on a low fat percentage. The foul odor in a few of the diarrhoea cases was at first thought to be due to decomposition of the ingested proteins. However, he quotes Fecr and Finkelstein, who have shown that almost none of the ingested proteins is found in the stools, and insist that the odor is due to the putrefaction of mucous and intestinal secretions and that the protein in the stools is derived from the nucleoproteins of the bile and the intestinal secretions.

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**The Condition of the Blood in Rickets.**—LEONARD FINDLAY (*Brit. Med. Jour.*, 1910, 1) studied the condition of the blood in rickets in children and also in puppies in which he had induced rickets experimentally. In 30 cases of active and uncomplicated rickets in children between twelve and fourteen months of age, only 9 showed any degree of anemia. In 2 of these the hemoglobin was only 5 per cent. below the accepted average, and the red cells in no instance were less than 4,100,000 per cubic millimeter. The majority of cases, on the other hand, gave high blood estimations so far as the hemoglobin and the number of red cells were concerned. Nucleated red corpuscles were seen on only one occasion. In only 2 cases was there an unequivocal leukocytosis, the white cells numbering 20,000 to 30,000 per cubic millimeter. Of the other 28 cases, 9 gave a normal or subnormal estimation, and in 19 the leukocytes were moderately increased in number, the maximum being 19,000 per cubic millimeter. Differential counts showed nothing characteristic. The results of the observations in experimental rickets in puppies were in entire accordance with those obtained in spontaneous rickets in children. When anemia was found it was minor in degree and was usually accounted for by some complication. Leukocytosis when present was also moderate and could usually be explained by some complication.

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**Intraventricular Injection of Flexner's Serum for Cerebrospinal Meningitis.**—LOUIS FISCHER (*Monthly Cycloped. and Med. Bulletin*, 1910, iii) reports a case of cerebrospinal meningitis in an infant, aged two months, which was treated by intraventricular injections of Flexner's

antimeningitis serum, with complete recovery. This method has so far not been successful in cases reported by Cushing, Netter, and others. The chief symptoms in the child were sudden onset with vomiting, rigidity of the head, neck, and extremities, and convulsive movements. The anterior fontanelle was open one-half inch and slightly bulging. On October 2, the first lumbar puncture resulted in 1 c.c. of turbid, blood-stained fluid which showed no meningococcus microscopically. The next three lumbar punctures resulted in dry taps, and as the fever, rigidity, opisthotonos and twitching were marked, the infant's lateral ventricles were tapped (October 20) and 15 c.c. of turbid fluid containing pus were withdrawn from the right ventricle. Smears taken from this fluid showed intracellular, Gram-negative meningococci. The ventricles were irrigated with normal saline solution at a temperature of 105° F. The excess fluid was drained out through the needle and 25 c.c. of Flexner's antimeningitis serum slowly injected into the ventricles. The infant changed in color from a waxy pallor to a uniform red flush all over the body, which persisted over half an hour with profuse perspiration. The temperature was 101° F., the respirations 80, and the pulse 120. On October 21 the ventricles were again irrigated, and 20 c.c. of the serum were injected. On October 22 the condition of the child was very poor. Opisthotonus was marked, and frequent paroxysms of muscular contractions occurred involving all its limbs. On October 23 a puncture below the fourth lumbar vertebra resulted in a dry tap. A second needle was inserted below the third lumbar vertebra and 15 c.c. of Flexner's serum injected through it, 3 c.c. returning through the first needle. Of 15 c.c. of serum then injected through the first needle, 5 c.c. returned through the second needle, showing that both needles were in the canal. In all, the infant retained about 25 c.c. of the serum in the spinal canal. A better result seemed to be obtained by using both the intraventricular method and the injections into the spinal canal. On October 25, 5 c.c. of slightly cloudy fluid was obtained by lumbar puncture. No meningococci were found in it, and 15 c.c. of the serum was injected into the spinal canal. On October 27, 20 c.c. of the serum was injected into the ventricles, although no fluid could be withdrawn. The total amount of Flexner's serum injected was about 105 c.c. The infant improved steadily from now on. On November 22, the right lateral ventricle was aspirated and 50 c.c. of clear fluid withdrawn which contained no meningococci and which resembled hydrocephalic fluid. The infant recovered without any complication on December 16. Fischer believes that if the ventricles cannot be drained by lumbar puncture, owing to a stasis or walling-in of ventricular or purulent fluid, and the symptoms persist, then the only way left is to tap the ventricles, flush with normal saline solution, and inject the antimeningitis serum as a specific. No danger was incurred in his case by piercing the frontal lobe and entering the ventricle, but rather relief was given to the symptoms of intracranial pressure. Flexner warns against injecting more fluid, that is, serum, than has been removed. The ventricles are aspirated in an infant through the anterior fontanelle. In older children the Kocher method is used, entering the skull by an incision over the second frontal convolution, and through it aspirating the ventricle.

**The Early Diagnosis of Infantile Scorbutus.**—HENRY KOPLIK (*Archiv of Diagnosis*, 1909, ii) states that scorbutus may develop in any infant whose food is or has been constructed on denutritional lines. It is a mistake to reject the possibility of scorbutus in a patient fed upon the breast or raw milk, since breast milk may have a denutritional composition, and raw milk be given in a denutritional state. Another element in the etiology of scorbutus is its intestinal source. The metabolism having become deranged, a development and invasion of toxins through the gut probably adds to the symptom complex. The ingestion of sterilized food in itself cannot explain all the phenomena of the disease, and many infants take sterilized food without developing scorbutus. The disease is uncommon in infants under five months. The first signs of incipient scorbutus are, a mild form of anemia, pain in the joints or bones elicited only by pressure, and the appearance of blood in the excretions or in the vicinity of bones or periosteum. In an otherwise perfectly healthy infant, fed on pasteurized milk, hematuria was the only gross symptom. Closer examination revealed a very mild anemia, a slight line of redness along the gums, and tenderness of the tibiæ only on deep pressure. Antiscorbutic treatment rapidly cleared up these symptoms, which otherwise would have developed a full picture of scorbutus. An infant, aged eleven months, was placed on a raw milk mixture containing excessive fat (7 per cent.). It gained satisfactorily until it developed a slight temperature above normal, a slight tenderness on manipulation of the left thigh and leg. The teeth and gums were normal except that there was a small, bluish-red cushion over the situation of the left lower canine, no tooth being felt. A diagnosis of osteomyelitis had been made, there being a high leukocyte count. The diagnosis was scorbutus (due to the excess of fat in the food), causing the pain in the thigh and hemorrhage in the left canine tooth-sac. Upon a proper food the infant made a complete recovery. It is not uncommon in infants of about six months who are apparently thriving, to find tenderness over the tibiæ on deep pressure. Such infants may have rickets, but the tenderness in question is scorbutic, and the test of correctness of the supposition is the rapid response to a change of diet aimed at warding off a full development of scorbutus.

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## GYNECOLOGY.

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**Spontaneous Rupture of Pyosalpinx into the General Peritoneal Cavity Producing Acute Diffuse Peritonitis.**—BONNEY (*Surg., Gyn., and Obst.*, 1909, ix, 542) has quite carefully studied the literature of this subject and from this study has concluded that: Spontaneous rupture of a

pyosalpinx or tubo-ovarian abscess into the general peritoneal cavity, producing acute fulminating peritonitis is a very rare accident. In the severity of its symptoms it usually resembles other forms of perforative peritonitis. It conforms to the general rule obtaining in such cases, that the earlier operation is performed, the greater is the chance of recovery. It is a very momentous accident, having a mortality of 30 per cent., even in those cases in which operation is made during the first twelve hours. It should be considered as the possible causative agent in all cases of acute general peritonitis of obscure origin occurring in females. Its proper treatment is immediate operation.

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**The Later Results of Ovariectomy.**—HOFMEIER (*Surg., Gyn., and Obst.*, 1909, ix, 381) carefully discussed the later results of ovariectomy, giving each pathological condition careful, though not exhaustive, consideration. Hofmeier believes fully 5 per cent. of ovarian carcinomas are secondary. He has operated on 59 cases of the ovary, in 43 of which but one ovary was involved. In 22 of the latter the affected ovary only was removed. The first of these is living, eighteen years after the operation. She bore a child one year after the operation and is now forty-five years of age. While Hofmeier believes operation should be performed in all cases in which removal seems possible, yet in unilateral involvement he recommends leaving the second ovary in young women. If both ovaries are involved, and then only, is removal of the uterus recommended. [Hofmeier's statistics in operation for cancer of the ovary are better than those of this country.—J. W. B.]

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**Abdominal Myomectomy for Large Uterine Fibroids.**—KUHN and FRICK (*Amer. Jour. Obst.*, 1909, ix, 443), after discussing the literature of hysterectomy and myomectomy for fibroids of the uterus, reports a series of ten successful myomectomies. In this paper are drawn the conclusions: (1) That myomectomy is especially indicated in women under forty years of age in which the genital tract can be left intact; (2) the limits of myomectomy should be extended under proper technique to cover part of the field of supravaginal hysterectomy; and, (3) myomectomy is the operation of choice for fibroids of the lower uterine segment in pregnancy.

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**Hemorrhagic Uteri; Myopathic Uterine Hemorrhage.**—B. H. ANSPACH (*Surg., Gyn., and Obst.*, 1909, ix, 315) believes the arteriosclerosis to which the terms "apoplexia uteri" and "intractable hemorrhage" have been applied is nothing more than a normal sclerosis and obliteration of the vascular channels of the uterus occurring in due proportion to the parity and the age of the individual. In only two of the cases reported in the literature or collected by Anspach were the uterine arteries calcified in a woman who had not passed the menopause. In these two exceptions the patients had reached the usual age for the occurrence of the menopause. The normal atrophy of the uterus, which begins about the time of the menopause, affects the muscle a little more than it does the connective tissue, but this plays no part in producing hemorrhage. Anspach believes the hemorrhages in conditions of this kind are due to fungous endometritis, hypertrophied and cystic cervix, displacement of the uterus, inflammatory lesions of the

adnexa or the cellular tissue of the pelvis, or congestion of the pelvic bloodvessels from general weakness, cardiac or renal disease.

**The Air of the Operation Room as a Possible Factor in the Infection of Wounds.**—H. ROBB (*Amer. Jour. Obst.*, 1909, lx, 451) has conducted a series of experiments to determine the relative infectivity of the air in his gynecological operating room in the Lakeside Hospital under varied conditions. The experiments were made in five series: (1) The floor was washed with a 1 to 1000 corrosive sublimate solution; (2) the washing was done with 1 to 20 carbolic acid solution; (3) with plain water; (4) no preparation of the floor was made; and (5) the series was composed of observations in other rooms and without any preparation of the floor. The use and non-use of a fan was also a feature of every series. Robb concludes that the use of antiseptics on the floor markedly lessened the number of bacteria in the air. More notable was the effect of the degree of cleanliness of the walls of the room. The effect of the fan was concluded to be nearly a negligible matter.

**Advantage of the Combined Intra- and Extraperitoneal Ureterolithotomy for the Removal of Stones from the Lower Ureter.**—JONAS (*Amer. Jour. Obst.*, 1909, lx, 728) believes the proper treatment for stone in the lower ureter is the combined intraperitoneal and extraperitoneal ureterolithotomy. The intraperitoneal part of the operation serves for exploration and for the removal of conditions which are possible etiological factors in the lodging and formation of stones. It also frequently makes the finding of the stone easier. The extraperitoneal steps serve for the removal of the stone. Stones higher up, at the crossing of the ureter and the iliac vessels can be removed by this combined route, as described and first emphasized by Gibbons. Should it be difficult to push the peritoneum back far enough, it might become necessary to add McBurney's gridiron incision. In this way, a flap is formed which gives complete access to the whole ureter from its point of crossing with the iliac vessels to the bladder. The shape of the entire incision is analogous to the cut described by Fowler for the extraperitoneal removal of ureteral stones in the lower ureter and now frequently advocated for the ligation of the common iliac artery.

## OTOLOGY.

UNDER THE CHARGE OF

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**The Ultimate Results of the Conservative Treatment of Chronic Suppurative Middle-ear Disease.**—VOGT (*Ztschr. f. Ohrenheilkunde*, 1909, lviii, 288).—The author's report is based upon the observation of 148 cases at least two and one-half years after cessation of treatment, those cases only being recorded as healed in which the discharge had entirely

ceased. The treatment, in the simple middle-ear cases included cleansing by means of normal salt solution followed by careful drying, removal of secretion by suction, the use of 10 per cent. boroglycerin, for the softening of the crusts, endonasal treatment, middle-ear irrigation through the tympanopharyngeal tube, in some cases ossiculectomy, instillation of solution of boric acid in alcohol with glycerin or of sublimate, touching with silver nitrate, and the insufflation of boric acid. In the cases with suppuration in the epitympanum the middle-ear syringe was used, and in all cases when indicated due attention was given to hygiene and to general medication. Of the 90 cases of simple suppurative middle-ear disease, 34 were healed and had so remained up to the time of observation; there had been 9 relapses, 32 had been improved, and 15 were unhealed. Of the 58 epitympanic cases, 23 were healed, there were 5 relapses, 21 were improved, and 9 were unhealed.

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**Quantitative Determination of Caloric Nystagmus in the Normal Labyrinth.**—KIPROFF (*Passows Beiträge*, 1909, ii, 129).—In order definitely to test the increase or decrease of excitability of the vestibular end apparatus, the determination of the vestibular reaction, in patients with normal labyrinths, was undertaken by the author by irrigation of the ear with water of a temperature of 86° F., the patient looking fixedly in a direction opposite to that of the irrigated ear, and the moment noted when the nystagmus began. This notation was effected by means of a stop watch started at the moment of commencement of irrigation, the moment when the nystagmus began being noted and the patient then directed to look straight forward, the moment of recurrence of the nystagmus being again noted, the irrigation being then immediately stopped, and a further time note made of the duration of the nystagmus, to the point of its complete disappearance. As the result of this examination, in 34 cases, a duration of irrigation, under the above-named conditions, with the eyes directed away from the irrigated ear, of from 15" to 45" was sufficient to induce nystagmus, but the investigation was continued also in cases both of non-suppurative and of suppurative middle-ear disease, in cases of total destruction of the drum head, of middle-ear suppuration after the radical operation, in inflammation of the external auditory canal, and in acute disease of the middle ear with the following results: The nystagmus symptoms appeared most speedily in the cases of total defect of the drum-head, with epidermatization of the labyrinth wall and in the cases which had undergone the radical operation; next in order came the normal cases, then the chronic suppurative cases, and finally, the acute suppurative and the cases of inflammation of the external canal. The average duration of the nystagmus was, in the normal and in the acute cases, from 1', 55" to 3', 5"; in the chronic suppurative and in the healed cases from 1', 25" to 2', 45".

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**Otosclerosis.**—THEODOR HEIMANN (*Sixteenth International Medical Congress*, Budapest, 1909, p. 183).—The conclusions drawn by the author, at the end of a long, carefully studied and critically presented statement of the present knowledge upon this subject, to which his now personal investigations have largely contributed, are as follows:

(1) The structural basis of the so-called otosclerosis consists in a bony ankylosis of the stapediovestibular joint. (2) From the anatomical pathological investigations so far made it would seem probable that the fixation of the stapes is the result of an inflammatory process of individual origin, which, while primarily it may have included the whole, or a large part, of the tympanic mucosa, has specially localized itself in the neighborhood of the labyrinth window. (3) While, from the observations thus far made, the supposition of a primary osteitis of the labyrinth capsule exhibiting itself in the region of the stapes cannot be excluded, the grounds for such a conception are not entirely conclusive, and do not sufficiently explain the considerable and progressive disturbance of hearing, without participation of the stapediovestibular articulation or the terminal nerve-ending apparatus of the labyrinth. (4) The sole and important cause of the disturbance of hearing, and other symptoms, in the so-called otosclerosis is a fixation of the stapes in the oval window, without differentiation as to the means by which this condition is brought about, whether originating in the middle ear, in the labyrinth, or existing as a congenital defect. (5) The principal cause of the otosclerosis must be regarded as a disturbance of general nutrition without reference to its origin. (6) Previous experience shows that heredity, anemia, syphilis, gestation, advanced age, and the female sex especially dispose to this disease, the cause of which in many cases remains unexplained. (7) Long and careful investigation would be required to determine whether or not this disease is dependent upon local causes, such as diseases of the upper respiratory tract, and particularly of the nose and nasopharynx. (8) The otosclerosis is to be regarded as the localization effect of a general disturbance of nutrition, evidencing itself in the ear. (9) The clinical picture of otosclerosis has, in certain cases, a strong resemblance to that occurring in the adhesive processes, of which fixation of the stapes is an accompaniment. (10) A definite therapeutic effect can be attained only by general treatment; local treatment is ineffective in the true primary cases of otosclerosis. (11) The expression otosclerosis, which corresponds neither to the structural nor to the clinical picture of this disease, and is liable to lead to misunderstanding, should be, with the corresponding term, "dry middle-ear catarrh," absolutely abandoned, and the title "periostitis ossificans stapediovestibularis" substituted for it. (12) Should further investigation determine that the disease originates primarily in the labyrinth capsule and is of inflammatory origin, the term "Ostitis vascularis stapediovestibularis" would be preferable.



## HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF

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**Vaccine Immunity.**—SÜPFLE (*Archiv f. Hygiene*, 1910, lxxviii, 301) closes an investigation of this subject with the following conclusions: (1) The local insertion of a vaccine results in only a local reproduction of the virus. (2) Immunity results from the gradual extension of the effects of the virus from the point of inoculation. (3) This immunity is histogenetic. (4) Cutaneous immunity results from either subcutaneous or intravenous vaccination. (5) Lymph heated to 60° induces, though not constantly, a cutaneous immunity. (6) When lymph is dialyzed, one obtains a dialysate which, when introduced subcutaneously, induces in many instances a partial immunity to subsequent cutaneous vaccination. (7) After cutaneous, subcutaneous, or intravenous inoculation the blood serum, sometimes, not constantly, contains antibodies which are capable of destroying the virus.

**The Poisonous Effects of Sodium Sulphite.**—KIONKA (*Archiv f. Hygiene*, lxxvii) found that continued feeding of small animals with moderate doses of sodium sulphite had no recognizable effect upon their growth or health, but after death he found many hemorrhagic spots in various organs and tissues. He killed his animals by washing out the blood-vessels with a dilute solution of indigoearmin. With the heart beating this coloring matter is supposed to be carried to all the tissues, but fails to reach any portions cut off by rupture of a vessel. On the other hand, hemorrhages would be recognized as dark blue spots. Lehmann and Trautwein (*Ibid.*, 68) have gone over this work, but suspecting that the hemorrhages might be due to the mode of death, killed their animals with chloroform slowly administered so as to avoid a death struggle. The animals employed were cats and dogs. The amount varied from 15 to 30 mg. per kilo per day, and the feeding was continued for two hundred days. The animals took the food containing the sulphite readily, grew normally, and at the end of the period appeared in perfect health. When killed no lesion, either macroscopic or microscopic, attributable to the sulphite, could be detected. The doses given were equivalent to from 3.7 to 18.7 grams of pure crystalline sodium sulphite per day to a man of 75 kilos. These investigators conclude that moderate amounts of sulphite may be absorbed from the stomach, oxidized to sulphate, and eliminated without harm to the individual. They are, however, careful to state that this finding should not be interpreted as supplying any justification of the use of sulphite as a preservative in meat. Sulphite is used as a preservative for chopped meats, such as the so-called Hamburger steaks, because it restores the color to putrid bits that could not be sold without this sophistication. This is the real and truly valid objections to its use.

**Nickel Utensils.**—LEHMANN (*Archiv. f. Hygiene*, lxviii, 421) has investigated the possibility of poisoning from cooking utensils made of nickel. Whether we will or not, we do get more or less of the widely distributed metals, as iron and copper, in our food, but this is not true of nickel. Some foods do take up small quantities of nickel when prepared in vessels made of this metal. Lehmann finds that if all the food eaten by a man be prepared in nickel he might get a maximum of 2 milligrams of the metal per kilo of body weight per day, and from his experiments on cats and dogs he concludes that this would do no harm.

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**Pseudomeningococci in the Throats of Healthy Children.**—In 8 per cent. of 150 school children examined, LIEBERKNECHT (*Archiv. f. Hygiene*, lxviii, 443) found pseudomeningococci. None of these children had been exposed to meningitis. With one exception, none of these organisms could be distinguished by cultural methods from the real meningococcus. This one gave a yellow growth on potato. At a temperature of 55° and after twenty-four hours they were agglutinated by specific serum in high dilution, while the serum of a normal rabbit had no effect, 1 to 20. On saccharine media these growths cannot be distinguished from the real. They grow well in pure culture on placental agar and in blood serum. On the addition of hematin to normal agar they grow abundantly and retain their vitality for a month. The addition of the saccharate of iron to ordinary or placental agar improves the growth on these media satisfactorily at either room or blood temperature.

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**On Being Tired.**—BRUNTON (*Practitioner*, lxxxiii, 409) discusses fatigue under the above title in his usual charming style. He seems inclined to the theory of Weichardt of fatigue toxins and antitoxins. However, he refers to the well-known custom of Alpine guides to prevent or relieve fatigue by taking food every two hours, and he thinks that the effect of food in relieving fatigue is so rapid that there is not time for absorption of the food, and that the action is an indirect one. The chemistry of the fatigue toxins has not been determined, but Brunton thinks them allied to ammonia or the compound ammonias. These are probably formed in the liver, or result there from the inability of the liver fully to convert ammonia salts into urea, the stimulus for which may be found in the intestinal walls. In addition to this the toxins may be formed by bacteria, such as the colon bacillus. The antitoxins may be greatly developed by proper training. Hard work produces fatigue toxins, and these in turn lead to the development of the antibodies. "I do not mean that it is right to assume that in nervous Americans worry produces fatigue, but it would almost seem so from the fact that they very commonly say, 'You make me tired,' instead of saying, 'you trouble' or 'you worry me.' One of the curious things about emotional fatigue is the rapidity with which it comes on, and this may possibly be explained by the fact that Weichardt found that the gray substance of the brain yields a fatigue toxin of great power." Cardiac dilatation is especially liable to occur in rapidly growing children, and is often the cause of the tired feeling of which they complain. This is one of the reasons why systematic physical

training should not be developed in the schools save under competent medical supervision. When the training is properly graded not only do the muscles become stronger and less easily fatigued, but the heart acquires additional strength. The famous wrestler Milo, of Crotona, carried a newly born calf day by day until it developed into a fully grown bull. Muscular training may help us to bear even that form of fatigue that comes from worry and mental depression. "Among all games, those of ball have been favorites, and they not only give pleasure and exercise to the muscles, but they tend to increase the power of coördination, which is of much more value than simple muscular power." There is a painting on an Egyptian tomb about 3500 years old, showing ladies tossing balls. "A very interesting problem may yet turn out to be the relationship between intestinal toxemia and the statement which has been put into the mouth of the unemployable British workman: 'I eats well, I drinks well, I sleeps well, but when I see a job of work coming along, I'm all of a tremble.'"

**Health in the Tropics.**—CHARLES (*Practitioner*, lxxxiv, 13) gives his experience in preserving the health of his family in India. Only boiled water should be used. Meat must come to the table straight from the fire. Alcohol is wholly unnecessary. Only those fruits that possess a rind that can be stripped off clean should be eaten. This excludes grapes, but permits oranges, bananas, apples, and pears. A filter should not be used, for its care is sure to be neglected. Clothing must be regulated by the temperature of the day and not by the season of the year. The "Kummerband," or abdominal binder of flannel, is not needed by a healthy man. Perfect cleanliness and the use of carbolic soap are the best prophylactics for the dhobie itch. Even in the hottest weather a light blanket should be provided, for about 3 A.M. there is a sudden fall in the temperature. Low shoes permit the mosquitos to bite the ankles, and top boots should be worn. Quinine and nets are necessary. When a man begins to worry he should leave the tropics, and only those in good health should go there. The Government gives one year's leave in five, and the Government would not do this had it not been found necessary.

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